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# INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

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) Title: 5' ESTs FOR SECRETED PROTEINS EXPRESS	CED IN	DDAG	
) Abstract	או ממכ	BRAIN	

The sequences of 5' ESTs derived from mRNAs encoding secreted proteins are disclosed. The 5' ESTs may be to obtain cDNAs and genomic DNAs corresponding to the 5' ESTs. The 5' ESTs may also be used in diagnostic, forensic, gene therapy, and chromosome expression vectors and secretion vectors.

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### (54) Title: 5' ESTs FOR SECRETED PROTEINS EXPRESSED IN BRAIN

#### (57) Abstract

The sequences of 5' ESTs derived from mRNAs encoding secreted proteins are disclosed. The 5' ESTs may be to obtain cDNAs and genomic DNAs corresponding to the 5' ESTs. The 5' ESTs may also be used in diagnostic, forensic, gene therapy, and chromosome mapping procedures. Upstream regulatory sequences may also be obtained using the 5' ESTs. The 5' ESTs may also be used to design expression vectors and secretion vectors.

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#### 5' ESTs FOR SECRETED PROTEINS EXPRESSED IN BRAIN

#### Background of the Invention

The estimated 50,000-100,000 genes scattered along the human chromosomes offer tremendous promise for the understanding, diagnosis, and treatment of human diseases. In addition, probes capable of specifically hybridizing to loci distributed throughout the human genome find applications in the construction of high resolution chromosome maps and in the identification of individuals.

In the past, the characterization of even a single human gene was a painstaking process, requiring years of effort. Recent developments in the areas of cloning vectors, DNA sequencing, and computer technology have merged to greatly accelerate the rate at which human genes can be isolated, sequenced, mapped, and characterized. Cloning vectors such as yeast artificial chromosomes (YACs) and bacterial artificial chromosomes (BACs) are able to accept DNA inserts ranging from 300 to 1000 kilobases (kb) or 100-400 kb in length respectively, thereby facilitating the manipulation and ordering of DNA sequences distributed over great distances on the human chromosomes. Automated DNA sequencing machines permit the rapid sequencing of human genes. Bioinformatics software enables the comparison of nucleic acid and protein sequences, thereby assisting in the characterization of human gene products.

Currently, two different approaches are being pursued for identifying and characterizing the genes distributed along the human genome. In one approach, large fragments of genomic DNA are isolated, cloned, and sequenced. Potential open reading frames in these genomic sequences are identified using bioinformatics software. However, this approach entails sequencing large stretches of human DNA which do not encode proteins in order to find the protein encoding sequences scattered throughout the genome. In addition to requiring extensive sequencing, the bioinformatics software may mischaracterize the genomic sequences obtained. Thus, the software may produce false positives in which non-coding DNA is mischaracterized as coding DNA or false negatives in which coding DNA is mischaracterized as non-coding DNA.

An alternative approach takes a more direct route to identifying and characterizing human genes. In this approach, complementary DNAs (cDNAs) are synthesized from isolated messenger RNAs (mRNAs) which encode human proteins. Using this approach,

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sequencing is only performed on DNA which is derived from protein coding portions of the genome. Often, only short stretches of the cDNAs are sequenced to obtain sequences called expressed sequence tags (ESTs). The ESTs may then be used to isolate or purify extended cDNAs which include sequences adjacent to the EST sequences. The extended cDNAs may contain all of the sequence of the EST which was used to obtain them or only a portion of the sequence of the EST which was used to obtain them. In addition, the extended cDNAs may contain the full coding sequence of the gene from which the EST was derived or, alternatively, the extended cDNAs may include portions of the coding sequence of the gene from which the EST was derived. It will be appreciated that there may be several extended cDNAs which include the EST sequence as a result of alternate splicing or the activity of alternative promoters.

In the past, these short EST sequences were often obtained from oligo-dT primed cDNA libraries. Accordingly, they mainly corresponded to the 3' untranslated region of the mRNA. In part, the prevalence of EST sequences derived from the 3' end of the mRNA is a result of the fact that typical techniques for obtaining cDNAs are not well suited for isolating cDNA sequences derived from the 5' ends of mRNAs. (Adams et al., Nature 377:3-174, 1996; Hillier et al., Genome Res. 6:807-828, 1996).

In addition, in those reported instances where longer cDNA sequences have been obtained, the reported sequences typically correspond to coding sequences and do not include the full 5' untranslated region of the mRNA from which the cDNA is derived. Such incomplete sequences may not include the first exon of the mRNA, particularly in situations where the first exon is short. Furthermore, they may not include some exons, often short ones, which are located upstream of splicing sites. Thus, there is a need to obtain sequences derived from the 5' ends of mRNAs.

While many sequences derived from human chromosomes have practical applications, approaches based on the identification and characterization of those chromosomal sequences which encode a protein product are particularly relevant to diagnostic and therapeutic uses. Of the 50,000-100,000 protein coding genes, those genes encoding proteins which are secreted from the cell in which they are synthesized, as well as the secreted proteins

themselves, are particularly valuable as potential therapeutic agents. Such proteins are often

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involved in cell to cell communication and may be responsible for producing a clinically relevant response in their target cells.

In fact, several secretory proteins, including tissue plasminogen activator, G-CSF, GM-CSF, erythropoietin, human growth hormone, insulin, interferon- $\alpha$ , interferon- $\beta$ , interferon- $\gamma$ , and interleukin-2, are currently in clinical use. These proteins are used to treat a wide range of conditions, including acute myocardial infarction, acute ischemic stroke, anemia, diabetes, growth hormone deficiency, hepatitis, kidney carcinoma, chemotherapy induced neutropenia and multiple sclerosis. For these reasons, extended cDNAs encoding secreted proteins or portions thereof represent a particularly valuable source of therapeutic agents. Thus, there is a need for the identification and characterization of secreted proteins and the nucleic acids encoding them.

In addition to being therapeutically useful themselves, secretory proteins include short peptides, called signal peptides, at their amino termini which direct their secretion. These signal peptides are encoded by the signal sequences located at the 5' ends of the coding sequences of genes encoding secreted proteins. Because these signal peptides will direct the extracellular secretion of any protein to which they are operably linked, the signal sequences may be exploited to direct the efficient secretion of any protein by operably linking the signal sequences to a gene encoding the protein for which secretion is desired. In addition, portions of signal sequences may also be used to direct the intracellular import of a peptide or protein of interest. This may prove beneficial in gene therapy strategies in which it is desired to deliver a particular gene product to cells other than the cell in which it is produced. Signal sequences encoding signal peptides also find application in simplifying protein purification techniques. In such applications, the extracellular secretion of the desired protein greatly facilitates purification by reducing the number of undesired proteins from which the desired protein must be selected. Thus, there exists a need to identify and characterize the 5' portions of the genes for secretory proteins which encode signal peptides

Public information on the number of human genes for which the promoters and upstream regulatory regions have been identified and characterized is quite limited. In part, this may be due to the difficulty of isolating such regulatory sequences. Upstream regulatory sequences such as transcription factor binding sites are typically too short to be utilized as probes for isolating promoters from human genomic libraries. Recently, some approaches

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have been developed to isolate human promoters. One of them consists of making a CpG island library (Cross, et al., Nature Genetics 6: 236-244, 1994). The second consists of isolating human genomic DNA sequences containing SpeI binding sites by the use of SpeI binding protein. (Mortlock et al., Genome Res. 6:327-335, 1996). Both of these approaches have their limits due to a lack of specificity or of comprehensiveness.

The present 5' ESTs may be used to efficiently identify and isolate upstream regulatory regions which control the location, developmental stage, rate, and quantity of protein synthesis, as well as the stability of the mRNA. (Theil, *BioFactors* 4:87-93, 1993). Once identified and characterized, these regulatory regions may be utilized in gene therapy or protein purification schemes to obtain the desired amount and locations of protein synthesis or to inhibit, reduce, or prevent the synthesis of undesirable gene products.

In addition, ESTs containing the 5' ends of secretory protein genes may include sequences useful as probes for chromosome mapping and the identification of individuals. Thus, there is a need to identify and characterize the sequences upstream of the 5' coding sequences of genes encoding secretory proteins.

#### Summary of the Invention

The present invention relates to purified, isolated, or recombinant ESTs which include sequences derived from the authentic 5' ends of their corresponding mRNAs. The term "corresponding mRNA" refers to the mRNA which was the template for the cDNA synthesis which produced the 5' EST. These sequences will be referred to hereinafter as "5' ESTs." As used herein, the term "purified" does not require absolute purity; rather, it is intended as a relative definition. Individual 5' EST clones isolated from a cDNA library have been conventionally purified to electrophoretic homogeneity. The sequences obtained from these clones could not be obtained directly either from the library or from total human DNA. The cDNA clones are not naturally occurring as such, but rather are obtained via manipulation of a partially purified naturally occurring substance (messenger RNA). The conversion of mRNA into a cDNA library involves the creation of a synthetic substance (cDNA) and pure individual cDNA clones can be isolated from the synthetic library by clonal selection. Thus, creating a cDNA library from messenger RNA and subsequently isolating individual clones from that library results in an approximately 10<sup>4</sup>-10<sup>6</sup> fold purification of the native message.

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Purification of starting material or natural material to at least one order of magnitude, preferably two or three orders, and more preferably four or five orders of magnitude is expressly contemplated.

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As used herein, the term "isolated" requires that the material be removed from its original environment (e.g., the natural environment if it is naturally occurring). For example, a naturally-occurring polynucleotide present in a living animal is not isolated, but the same polynucleotide, separated from some or all of the coexisting materials in the natural system, is isolated.

As used herein, the term "recombinant" means that the 5' EST is adjacent to "backbone" nucleic acid to which it is not adjacent in its natural environment. Additionally, to be "enriched" the 5' ESTs will represent 5% or more of the number of nucleic acid inserts in a population of nucleic acid backbone molecules. Backbone molecules according to the present invention include nucleic acids such as expression vectors, self-replicating nucleic acids, viruses, integrating nucleic acids, and other vectors or nucleic acids used to maintain or manipulate a nucleic acid insert of interest. Preferably, the enriched 5' ESTs represent 15% or more of the number of nucleic acid inserts in the population of recombinant backbone molecules. More preferably, the enriched 5' ESTs represent 50% or more of the number of nucleic acid inserts in the population of recombinant backbone molecules. In a highly preferred embodiment, the enriched 5' ESTs represent 90% or more of the number of nucleic acid inserts in the population of recombinant backbone molecules.

"Stringent", moderate," and "low" hybridization conditions are as defined in Example 29.

Unless otherwise indicated, a "complementary" sequence is fully complementary.

Thus, 5' ESTs in cDNA libraries in which one or more 5' ESTs make up 5% or more of the number of nucleic acid inserts in the backbone molecules are "enriched recombinant 5" ESTs" as defined herein. Likewise, 5' ESTs in a population of plasmids in which one or more 5' EST of the present invention have been inserted such that they represent 5% or more of the number of inserts in the plasmid backbone are " enriched recombinant 5' ESTs" as defined herein. However, 5' ESTs in cDNA libraries in which 5' ESTs constitute less than 5% of the number of nucleic acid inserts in the population of backbone molecules, such as libraries in

which backbone molecules having a 5' EST insert are extremely rare, are not "enriched recombinant 5' ESTs."

In particular, the present invention relates to 5' ESTs which are derived from genes encoding secreted proteins. As used herein, a "secreted" protein is one which, when expressed in a suitable host cell, is transported across or through a membrane, including transport as a result of signal peptides in its amino acid sequence. "Secreted" proteins include without limitation proteins secreted wholly (e.g. soluble proteins), or partially (e.g. receptors) from the cell in which they are expressed. "Secreted" proteins also include without limitation proteins which are transported across the membrane of the endoplasmic reticulum.

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Such 5' ESTs include nucleic acid sequences, called signal sequences, which encode signal peptides which direct the extracellular secretion of the proteins encoded by the genes from which the 5' ESTs are derived. Generally, the signal peptides are located at the amino termini of secreted proteins.

Secreted proteins are translated by ribosomes associated with the "rough" endoplasmic reticulum. Generally, secreted proteins are co-translationally transferred to the membrane of the endoplasmic reticulum. Association of the ribosome with the endoplasmic reticulum during translation of secreted proteins is mediated by the signal peptide. The signal peptide is typically cleaved following its co-translational entry into the endoplasmic reticulum. After delivery to the endoplasmic reticulum, secreted proteins may proceed through the Golgi apparatus. In the Golgi apparatus, the proteins may undergo post-translational modification before entering secretory vesicles which transport them across the cell

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membrane.

The 5' ESTs of the present invention have several important applications. For example, they may be used to obtain and express cDNA clones which include the full protein coding sequences of the corresponding gene products, including the authentic translation start sites derived from the 5' ends of the coding sequences of the mRNAs from which the 5' ESTs are derived. These cDNAs will be referred to hereinafter as "full length cDNAs." These cDNAs may also include DNA derived from mRNA sequences upstream of the translation start site. The full length cDNA sequences may be used to express the proteins corresponding to the 5' ESTs. As discussed above, secreted proteins are therapeutically important. Thus, the proteins expressed from the cDNAs may be useful in treating or

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controlling a variety of human conditions. The 5' ESTs may also be used to obtain the corresponding genomic DNA. The term "corresponding genomic DNA" refers to the genomic DNA which encodes the mRNA from which the 5' EST was derived.

Alternatively, the 5' ESTs may be used to obtain and express extended cDNAs encoding portions of the secreted protein. The portions may comprise the signal peptides of the secreted proteins or the mature proteins generated when the signal peptide is cleaved off. The portions may also comprise polypeptides having at least 10 consecutive amino acids encoded by the extended cDNAs or full length cDNAs. Alternatively, the portions may comprise at least 15 consecutive amino acids encoded by the extended cDNAs or full length cDNAs. In some embodiments, the portions may comprise at least 25 consecutive amino acids encoded by the extended cDNAs or full length cDNAs. In other embodiments, the portions may comprise at least 40 amino acids encoded by the extended cDNAs or full length cDNAs.

Antibodies which specifically recognize the entire secreted proteins encoded by the extended cDNAs, full length cDNAs, or fragments thereof having at least 10 consecutive amino acids, at least 15 consecutive amino acids, at least 25 consecutive amino acids, or at least 40 consecutive amino acids may also be obtained as described below. Antibodies which specifically recognize the mature protein generated when the signal peptide is cleaved may also be obtained as described below. Similarly, antibodies which specifically recognize the signal peptides encoded by the extended cDNAs or full length cDNAs may also be obtained.

In some embodiments, the extended cDNAs obtained using the 5' ESTs include the signal sequence. In other embodiments, the extended cDNAs obtained using the 5' ESTs may include the full coding sequence for the mature protein (*i.e.* the protein generated when the signal polypeptide is cleaved off). In addition, the extended cDNAs obtained using the 5' ESTs may include regulatory regions upstream of the translation start site or downstream of the stop codon which control the amount, location, or developmental stage of gene expression.

As discussed above, secreted proteins are therapeutically important. Thus, the proteins expressed from the extended cDNAs or full length cDNAs obtained using the 5' ESTs may be useful in treating or controlling a variety of human conditions.

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The 5' ESTs (or cDNAs or genomic DNAs obtained therefrom) may be used in forensic procedures to identify individuals or in diagnostic procedures to identify individuals having genetic diseases resulting from abnormal expression of the genes corresponding to the 5' ESTs. In addition, the present invention is useful for constructing a high resolution map of the human chromosomes.

The present invention also relates to secretion vectors capable of directing the secretion of a protein of interest. Such vectors may be used in gene therapy strategies in which it is desired to produce a gene product in one cell which is to be delivered to another location in the body. Secretion vectors may also facilitate the purification of desired proteins.

The present invention also relates to expression vectors capable of directing the expression of an inserted gene in a desired spatial or temporal manner or at a desired level. Such vectors may include sequences upstream of the 5' ESTs, such as promoters or upstream regulatory sequences.

Finally, the present invention may also be used for gene therapy to control or treat genetic diseases. Signal peptides may also be fused to heterologous proteins to direct their extracellular secretion.

Bacterial clones containing Bluescript plasmids having inserts containing the 5' ESTs of the present invention (SEQ ID NOs: 38-270 are presently stored at 80°C in 4% (v/v) glycerol in the inventor's laboratories under the designations listed next to the SEQ ID NOs in II). The inserts may be recovered from the deposited materials by growing the appropriate clones on a suitable medium. The Bluescript DNA can then be isolated using plasmid isolation procedures familiar to those skilled in the art such as alkaline lysis minipreps or large scale alkaline lysis plasmid isolation procedures. If desired the plasmid DNA may be further enriched by centrifugation on a cesium chloride gradient, size exclusion chromatography, or anion exchange chromatography. The plasmid DNA obtained using these procedures may then be manipulated using standard cloning techniques familiar to those skilled in the art. Alternatively, a PCR can be done with primers designed at both ends of the EST insertion. The PCR product which corresponds to the 5' EST can then be manipulated using standard cloning techniques familiar to those skilled in the art.

One aspect of the present invention is a purified or isolated nucleic acid having the sequence of one of SEQ ID NOs: 38-270 or having a sequence complementary thereto. In one embodiment, the nucleic acid is recombinant.

Another aspect of the present invention is a purified or isolated nucleic acid comprising at least 10 consecutive bases of the sequence of one of SEQ ID NOs: 38-270 or one of the sequences complementary thereto.

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Yet another aspect of the present invention is a purified or isolated nucleic acid comprising at least 15 consecutive bases of one of the sequences of SEQ ID NOs: 38-270 or one of the sequences complementary thereto. In one embodiment, the nucleic acid is recombinant.

A further aspect of the present invention is a purified or isolated nucleic acid of at least 15 bases capable of hybridizing under stringent conditions to the sequence of one of SEQ ID NOs: 38-270 or one of the sequences complementary to the sequences of SEQ ID NOs: 38-270. In one embodiment, the nucleic acid is recombinant.

Another aspect of the present invention is a purified or isolated nucleic acid encoding a human gene product, said human gene product having a sequence partially encoded by one of the sequences of SEQ ID NO: 38-270.

Still another aspect of the present invention is a method of making a cDNA encoding a human secretory protein, said human secretory protein being partially encoded by one of SEQ ID NOs 38-270, comprising the steps of contacting a collection of mRNA molecules from human cells with a primer comprising at least 15 consecutive nucleotides of a sequence complementary to one of SEQ ID NOs: 38-270; hybridizing said primer to an mRNA in said collection that encodes said protein; reverse transcribing said hybridized primer to make a first cDNA strand from said mRNA; making a second cDNA strand complementary to said first cDNA strand; and isolating the resulting cDNA encoding said protein comprising said first cDNA strand and said second cDNA strand.

Another aspect of the invention is an isolated or purified cDNA encoding a human secretory protein, said human secretory protein comprising the protein encoded by one of SEQ ID NOs 38-270 or a fragment thereof of at least 10 amino acids, said cDNA being obtainable by the method described in the preceding paragraph. In one embodiment, the

cDNA comprises the full protein coding sequence of said protein which sequence is partially included in one of the sequences of SEQ ID NOs: 38-270.

Another aspect of the present invention is a method of making a cDNA encoding a human secretory protein that is partially encoded by one of SEQ ID NOs 38-270, comprising the steps of obtaining a cDNA comprising one of the sequences of SEQ ID NOs: 38-270, contacting said cDNA with a detectable probe comprising at least 15 consecutive nucleotides of said sequence of SEQ ID NO: 38-270 or a sequence complementary thereto under conditions which permit said probe to hybridize to said cDNA; identifying a cDNA which hybridizes to said detectable probe; and isolating said cDNA which hybridizes to said probe.

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Another aspect of the present invention is an isolated or purified cDNA encoding a human secretory protein, said human secretory protein comprising the protein encoded by one of SEQ ID NOs 38-270 or a fragment thereof of at least 10 amino acids, said cDNA being obtainable by the method described in the preceding paragraph. In one embodiment, the cDNA comprises the full protein coding sequence partially included in one of the sequences of SEQ ID NOs: 38-270.

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Another aspect of the present invention is a method of making a cDNA comprising one of the sequence of SEQ ID NOs: 38-270, comprising the steps of contacting a collection of mRNA molecules from human cells with a first primer capable of hybridizing to the polyA tail of said mRNA; hybridizing said first primer to said polyA tail; reverse transcribing said mRNA to make a first cDNA strand; making a second cDNA strand complementary to said first cDNA strand using at least one primer comprising at least 15 nucleotides of one of the sequences of SEQ ID NOs 38-270; and isolating the resulting cDNA comprising said first cDNA strand and said second cDNA strand.

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Another aspect of the present invention is an isolated or purified cDNA encoding a human secretory protein, said human secretory protein comprising the protein encoded by one of SEQ ID NOs 38-270 or a fragment thereof of at least 10 amino acids, said cDNA being obtainable by the method described in the preceding paragraph. In one embodiment, the cDNA comprises the full protein coding sequence partially included in one of the sequences of SEQ ID NOs: 38-270.

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In one embodiment of the method described in the two paragraphs above, the second cDNA strand is made by contacting said first cDNA strand with a first pair of primers, said

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first pair of primers comprising a second primer comprising at least 15 consecutive nucleotides of one of the sequences of SEQ ID NOs 38-270 and a third primer having a sequence therein which is included within the sequence of said first primer; performing a first polymerase chain reaction with said first pair of nested primers to generate a first PCR product; contacting said first PCR product with a second pair of primers, said second pair of primers comprising a fourth primer, said fourth primer comprising at least 15 consecutive nucleotides of said sequence of one of SEQ ID NOs: 38-270, and a fifth primer, said fourth and fifth primers being capable of hybridizing to sequences within said first PCR product; and performing a second polymerase chain reaction, thereby generating a second PCR product.

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One aspect of the present invention is an isolated or purified cDNA encoding a human secretory protein, said human secretory protein comprising the protein encoded by one of SEQ ID NOs 38-270, or a fragment thereof of at least 10 amino acids, said cDNA being obtainable by the method of the preceding paragraph. In one embodiment, the cDNA comprises the full protein coding sequence partially included in one of the sequences of SEQ ID NOs: 38-270.

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Another aspect of the present invention is the method described four paragraphs above in which the second cDNA strand is made by contacting said first cDNA strand with a second primer comprising at least 15 consecutive nucleotides of the sequences of SEQ ID NOs: 38-270, hybridizing said second primer to said first strand cDNA; and extending said hybridized second primer to generate said second cDNA strand.

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Another aspect of the present invention is an isolated or purified cDNA encoding a human secretory protein, said human secretory protein comprising the protein partially encoded by one of SEQ ID NOs 38-270 or comprising a fragment thereof of at least 10 amino acids, said cDNA being obtainable by the method described in the preceding paragraph. In one embodiment, the cDNA comprises the full protein coding sequence partially included in of one of the sequences of SEQ ID NOs: 38-270.

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Another aspect of the present invention is a method of making a protein comprising one of the sequences of SEQ ID NOs: 271-503, comprising the steps of obtaining a cDNA encoding the full protein sequence partially included in one of the sequences of sequence of SEQ ID NOs: 38-270; inserting said cDNA in an expression vector such that said cDNA is

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operably linked to a promoter; introducing said expression vector into a host cell whereby said host cell produces the protein encoded by said cDNA; and isolating said protein.

Another aspect of the present invention is an isolated protein obtainable by the method described in the preceding paragraph.

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Another aspect of the present invention is a method of obtaining a promoter DNA comprising the steps of obtaining DNAs located upstream of the nucleic acids of SEQ ID NOs: 38-270 or the sequences complementary thereto; screening said upstream DNAs to identify a promoter capable of directing transcription initiation; and isolating said DNA comprising said identified promoter. In one embodiment, the obtaining step comprises chromosome walking from said nucleic acids of SEQ ID NOs: 38-270 or sequences complementary thereto. In another embodiment, the screening step comprises inserting said upstream sequences into a promoter reporter vector. In another embodiment, the screening step comprises identifying motifs in said upstream DNAs which are transcription factor binding sites or transcription start sites.

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Another aspect of the present invention is an isolated promoter obtainable by the method described above.

Another aspect of the present invention is an isolated or purified protein comprising one of the sequences of SEQ ID NOs: 271-503.

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Another aspect of the present invention is the inclusion of at least one of the sequences of SEQ ID NOs: 38-270, or one of the sequences complementary to the sequences of SEQ ID NOs: 38-270, or a fragment thereof of at least 15 consecutive nucleotides in an array of discrete ESTs or fragments thereof of at least 15 nucleotides in length. In one embodiment, the array includes at least two of the sequences of SEQ ID NOs: 38-270, the sequences complementary to the sequences of SEQ ID NOs: 38-270, or fragments thereof of at least 15 consecutive nucleotides. In another embodiment, the array includes at least five of the sequences of SEQ ID NOs: 38-270, the sequences complementary to the sequences of SEQ ID NOs: 38-270, or fragments thereof of at least 15 consecutive nucleotides.

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Another aspect of the present invention is a promoter having a sequence selected from the group consisting of SEQ ID NOs: 31, 34, and 37.

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# Brief Description of the Drawings

Figure 1 is a summary of a procedure for obtaining cDNAs which have been selected to include the 5' ends of the mRNAs from which they derived.

Figure 2 shows the distribution of Von Heijne scores for 5' ESTs in each of the categories described herein and the probability that these 5' ESTs encode a signal peptide.

Figure 3 summarizes a general method used to clone and sequence extended cDNAs containing sequences adjacent to 5' ESTs.

Figure 4 (description of promoters structure isolated from SignalTag 5' ESTs) provides a schematic description of promoters isolated and the way they are assembled with the corresponding 5' tags.

# **Detailed Description of the Preferred Embodiment**

Table IV is an analysis of the 43 amino acids located at the N terminus of all human SwissProt proteins to determine the frequency of false positives and false negatives using the techniques for signal peptide identification described herein.

Table V shows the distribution of 5' ESTs in each category described herein and the number of 5' ESTs in each category having a given minimum Von Heijne's score.

Table VI shows the distribution of 5' ESTs in each category described herein with respect to the tissue from which the 5' ESTs of the corresponding mRNA were obtained.

Table VII describes the transcription factor binding sites present in each of these promoters.

# I. General Methods for Obtaining 5' ESTs derived from mRNAs with intact 5' ends

In order to obtain the 5' ESTs of the present invention, mRNAs with intact 5' ends must be obtained. Currently, there are two approaches for obtaining such mRNAs with intact 5' ends as described below: either chemical (1) or enzymatic (2).

# 1. Chemical Methods for Obtaining mRNAs having Intact 5' Ends

One of these approaches is a chemical modification method involving derivatization of the 5' ends of the mRNAs and selection of the derivatized mRNAs. The 5' ends of eukaryotic mRNAs possess a structure referred to as a "cap" which comprises a guanosine

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methylated at the 7 position. The cap is joined to the first transcribed base of the mRNA by a 5', 5'-triphosphate bond. In some instances, the 5' guanosine is methylated in both the 2 and 7 positions. Rarely, the 5' guanosine is trimethylated at the 2, 7 and 7 positions. In the chemical method for obtaining mRNAs having intact 5' ends, the 5' cap is specifically derivatized and coupled to a reactive group on an immobilizing substrate. This specific derivatization is based on the fact that only the ribose linked to the methylated guanosine at the 5' end of the mRNA and the ribose linked to the base at the 3' terminus of the mRNA, possess 2', 3'-cis diols.

Optionally, the 2', 3'-cis diol of the 3' terminal ribose may be chemically modified, substituted, converted, or eliminated, leaving only the ribose linked to the methylated guanosine at the 5' end of the mRNA with a 2', 3'-cis diol. A variety of techniques are available for eliminating the 2', 3'-cis diol on the 3' terminal ribose. For example, controlled alkaline hydrolysis may be used to generate mRNA fragments in which the 3' terminal ribose is a 3'-phosphate, 2'-phosphate or (2', 3')-cyclophosphate. Thereafter, the fragment which includes the original 3' ribose may be eliminated from the mixture through chromatography on an oligodT column. Alternatively, a base which lacks the 2', 3'-cis diol may be added to the 3' end of the mRNA using an RNA ligase such as T4 RNA ligase. Example 1 below describes a method for ligation of a nucleoside diphosphate to the 3' end of messenger RNA.

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#### **EXAMPLE 1**

#### Ligation of the Nucleoside Diphosphate pCp to the 3' End of mRNA.

One µg of RNA was incubated in a final reaction medium of 10 µl in the presence of 5 U of T<sub>4</sub> phage RNA ligase in the buffer provided by the manufacturer (Gibco - BRL), 40 U of the RNase inhibitor RNasin (Promega) and, 2 µl of <sup>32</sup>pCp (Amersham #PB 10208). The incubation was performed at 37°C for 2 hours or overnight at 7-8°C.

Following modification or elimination of the 2', 3'-cis diol at the 3' ribose, the 2', 3'-cis diol present at the 5' end of the mRNA may be oxidized using reagents such as NaBH, NaBH<sub>3</sub>CN, or sodium periodate, thereby converting the 2', 3'-cis diol to a dialdehyde. Example 2 describes the oxidation of the 2', 3'-cis diol at the 5' end of the mRNA with sodium periodate.

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#### **EXAMPLE 2**

#### Oxidation of 2', 3'-cis diol at the 5' End of the mRNA with Sodium Periodate

0.1 OD unit of either a capped oligoribonucleotide of 47 nucleotides (including the cap) or an uncapped oligoribonucleotide of 46 nucleotides were treated as follows. The oligoribonucleotides were produced by *in vitro* transcription using the transcription kit "AmpliScribe T7" (Epicentre Technologies). As indicated below, the DNA template for the RNA transcript contained a single cytosine. To synthesize the uncapped RNA, all four NTPs were included in the *in vitro* transcription reaction. To obtain the capped RNA, GTP was replaced by an analogue of the cap, m7G(5')ppp(5')G. This compound, recognized by the polymerase, was incorporated into the 5' end of the nascent transcript during the initiation of transcription but was not incorporated during the extension step. Consequently, the resulting RNA contained a cap at its 5' end. The sequences of the oligoribonucleotides produced by the *in vitro* transcription reaction were:

+Cap:

5'm7GpppGCAUCCUACUCCCAUCCAAUUCCACCCUAACUCCUCCCAUCUCCAC-3' (SEQ ID NO:1)

-Cap:

5'-pppGCAUCCUACUCCAUCCAAUUCCACCUAACUCCUCCCAUCUCCAC-3' (SEQ ID NO:2)

The oligoribonucleotides were dissolved in 9 µl of acetate buffer (0.1 M sodium acetate, pH 5.2) and 3 µl of freshly prepared 0.1 M sodium periodate solution. The mixture was incubated for 1 hour in the dark at 4°C or room temperature. Thereafter, the reaction was stopped by adding 4 µl of 10% ethylene glycol. The product was ethanol precipitated, resuspended in at least 10 µl of water or appropriate buffer and dialyzed against water.

The resulting aldehyde groups may then be coupled to molecules having a reactive amine group, such as hydrazine, carbazide, thiocarbazide or semicarbazide groups, in order to facilitate enrichment of the 5' ends of the mRNAs. Molecules having reactive amine groups which are suitable for use in selecting mRNAs having intact 5' ends include avidin, proteins, antibodies, vitamins, ligands capable of specifically binding to receptor molecules, or oligonucleotides. Example 3 below describes the coupling of the resulting dialdehyde to biotin.

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#### **EXAMPLE 3**

### Coupling of the Dialdehyde at the 5' End of Transcripts with Biotin

The oxidation product obtained in Example 2 was dissolved in 50  $\mu$ l of sodium acetate at a pH between 5 and 5.2 and 50  $\mu$ l of freshly prepared 0.02 M solution of biotin hydrazide in a methoxyethanol/water mixture (1:1) of formula:

In the compound used in these experiments, n=5. However, it will be appreciated that other commercially available hydrazides may also be used, such as molecules of the above formula in which n varies from 0 to 5. The mixture was then incubated for 2 hours at 37°C, precipitated with ethanol and dialyzed against distilled water. Example 4 demonstrates the specificity of the biotinylation reaction.

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#### **EXAMPLE 4**

#### Specificity of Biotinylation of Capped Transcripts

The specificity of the biotinylation for capped mRNAs was evaluated by gel electrophoresis of the following samples:

- Sample 1. The 46 nucleotide uncapped *in vitro* transcript prepared as in Example 2 and labeled with <sup>32</sup>pCp as described in Example 1.
- Sample 2. The 46 nucleotide uncapped *in vitro* transcript prepared as in Example 2, labeled with <sup>32</sup>pCp as described in Example 1, treated with the oxidation reaction of Example 2, and subjected to the biotinylation conditions of Example 3.
- Sample 3. The 47 nucleotide capped *in vitro* transcript prepared as in Example 2 and labeled with <sup>32</sup>pCp as described in Example 1.

Sample 4. The 47 nucleotide capped *in vitro* transcript prepared as in Example 2, labeled with <sup>32</sup>pCp as described in Example 1, treated with the oxidation reaction of Example 2, and subjected to the biotinylation conditions of Example 3.

Samples 1 and 2 had identical migration rates, demonstrating that the uncapped RNAs were not oxidized and biotinylated. Sample 3 migrated more slowly than Samples 1 and 2, while Sample 4 exhibited the slowest migration. The difference in migration of the RNAs in Samples 3 and 4 demonstrates that the capped RNAs were specifically biotinylated.

In some cases, mRNAs having intact 5' ends may be enriched by binding the molecule containing a reactive amine group to a suitable solid phase substrate such as the inside of the vessel containing the mRNAs, magnetic beads, chromatography matrices, or nylon or nitrocellulose membranes. For example, where the molecule having a reactive amine group is biotin, the solid phase substrate may be coupled to avidin or streptavidin. Alternatively, where the molecule having the reactive amine group is an antibody or receptor ligand, the solid phase substrate may be coupled to the cognate antigen or receptor. Finally, where the molecule having a reactive amine group comprises an oligonucleotide, the solid phase substrate may comprise a complementary oligonucleotide.

The mRNAs having intact 5' ends may be released from the solid phase following the enrichment procedure. For example, where the dialdehyde is coupled to biotin hydrazide and the solid phase comprises streptavidin, the mRNAs may be released from the solid phase by simply heating to 95 degrees Celsius in 2% SDS. In some methods, the molecule having a reactive amine group may also be cleaved from the mRNAs having intact 5' ends following enrichment. Example 5 describes the capture of biotinylated mRNAs with streptavidin coated beads and the release of the biotinylated mRNAs from the beads following enrichment.

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#### Capture and Release of Biotinylated mRNAs Using Streptavidin Coated Beads

The streptavidin coated magnetic beads were prepared according to the manufacturer's instructions (CPG Inc., USA). The biotinylated mRNAs were added to a hybridization buffer (1.5 M NaCl, pH 5 - 6). After incubating for 30 minutes, the unbound and nonbiotinylated material was removed. The beads were then washed several times in

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water with 1% SDS. The beads thus obtained were incubated for 15 minutes at 95°C in water containing 2% SDS.

Example 6 demonstrates the efficiency with which biotinylated mRNAs were recovered from the streptavidin coated beads.

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#### **EXAMPLE 6**

### Efficiency of Recovery of Biotinylated mRNAs

The efficiency of the recovery procedure was evaluated as follows. Capped RNAs were labeled with <sup>32</sup>pCp, oxidized, biotinylated and bound to streptavidin coated beads as described above. Subsequently, the bound RNAs were incubated for 5, 15 or 30 minutes at 95°C in the presence of 2% SDS.

The products of the reaction were analyzed by electrophoresis on 12% polyacrylamide gels under denaturing conditions (7 M urea). The gels were subjected to autoradiography. During this manipulation, the hydrazone bonds were not reduced.

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Increasing amounts of nucleic acids were recovered as incubation times in 2% SDS increased, demonstrating that biotinylated mRNAs were efficiently recovered.

In an alternative method for obtaining mRNAs having intact 5' ends, an oligonucleotide which has been derivatized to contain a reactive amine group is specifically coupled to mRNAs having an intact cap. Preferably, the 3' end of the mRNA is blocked prior to the step in which the aldehyde groups are joined to the derivatized oligonucleotide, as described above, so as to prevent the derivatized oligonucleotide from being joined to the 3' end of the mRNA. For example, pCp may be attached to the 3' end of the mRNA using T4 RNA ligase as described in example 1. However, as discussed above, blocking the 3' end of the mRNA is an optional step. Derivatized oligonucleotides may be prepared as described in Example 7.

#### **EXAMPLE 7**

#### **Derivatization of Oligonucleotides**

An oligonucleotide phosphorylated at its 3' end was converted to a 3' hydrazide in 3' by treatment with an aqueous solution of hydrazine or of dihydrazide of the formula  $H_2N(R1)NH_2$  at about 1 to 3 M, and at pH 4.5 at a temperature of 8°C overnight. This

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incubation was performed in the presence of a carbodiimide type agent soluble in water such as 1-ethyl-3-(3-dimethylaminopropyl)carbodiimide at a final concentration of 0.3 M.

The derivatized oligonucleotide was then separated from the other agents and products using a standard technique for isolating oligonucleotides.

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As discussed above, the mRNAs to be enriched may be treated to eliminate the 3' OH groups which may be present thereon. This may be accomplished by enzymatic ligation of sequences lacking a 3' OH, such as pCp, as described in Example 1. Alternatively, the 3' OH groups may be eliminated by alkaline hydrolysis as described in Example 8 below.

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#### **EXAMPLE 8**

# Elimination of 3' OH Groups of mRNA Using Alkaline Hydrolysis

In a total volume of 100  $\mu$ l of 0.1 N sodium hydroxide, 1.5  $\mu$ g mRNA is incubated for 40 to 60 minutes at 4°C. The solution is neutralized with acetic acid and precipitated with ethanol.

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Following the optional elimination of the 3' OH groups, the diol groups at the 5' ends of the mRNAs are oxidized as described below in Example 9.

#### **EXAMPLE 9**

### Oxidation of Diols of mRNA

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Up to 1 OD unit of RNA was dissolved in 9  $\mu$ l of buffer (0.1 M sodium acetate, pH 6-7) or water and 3  $\mu$ l of freshly prepared 0.1 M sodium periodate solution. The reaction was incubated for 1 h in the dark at 4°C or room temperature. Following the incubation, the reaction was stopped by adding 4  $\mu$ l of 10% ethylene glycol. Thereafter the mixture was incubated at room temperature for 15 minutes. After ethanol precipitation, the product was resuspended in at least 10  $\mu$ l of water or appropriate buffer and dialyzed against water.

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Following oxidation of the diol groups at the 5' ends of the mRNAs, the derivatized oligonucleotide was joined to the resulting aldehydes as described in Example 10.

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#### **EXAMPLE 10**

#### Ligature of Aldehydes of mRNA to Derivatized Oligonucleotides

The oxidized mRNA was dissolved in an acidic medium such as 50 µl of sodium acetate pH 4-6. Fifty µl of a solution of the derivatized oligonucleotide were added in order to obtain an mRNA:derivatized oligonucleotide ratio of 1:20. The mixture was reduced with a borohydride and incubated for 2 h at 37°C or overnight (14 h) at 10°C. The mixture was then ethanol precipitated, resuspended in 10 µl or more of water or appropriate buffer and dialyzed against distilled water. If desired, the resulting product may be analyzed using acrylamide gel electrophoresis, HPLC analysis, or other conventional techniques.

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Following the attachment of the derivatized oligonucleotide to the mRNAs, a reverse transcription reaction may be performed as described in Example 11 below.

#### **EXAMPLE 11**

### Reverse Transcription of mRNAs Ligatured to Derivatized Oligonucleotides

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An oligodeoxyribonucleotide was derivatized as follows. Three OD units of an oligodeoxyribonucleotide of sequence 5'ATCAAGAATTCGCACGAGACCATTA3' (SEQ ID NO:3) having 5'-OH and 3'-P ends were dissolved in 70 µl of a 1.5 M hydroxybenzotriazole solution, pH 5.3, prepared in dimethylformamide/water (75:25) containing 2 µg of 1-ethyl-3-(3-dimethylaminopropyl)carbodiimide. The mixture was incubated for 2 h 30 min at 22°C and then precipitated twice in LiClO<sub>4</sub>/acetone. The pellet was resuspended in 200 µl of 0.25 M hydrazine and incubated at 8°C from 3 to 14 h. Following the hydrazine reaction, the mixture was precipitated twice in LiClO<sub>4</sub>/acetone.

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The messenger RNAs to be reverse transcribed were extracted from blocks of placenta having sides of 2 cm which had been stored at -80°C. The total RNA was extracted using conventional acidic phenol techniques. Oligo-dT chromatography was used to purify the mRNAs. The integrity of the mRNAs was checked by Northern-blotting.

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The diol groups on 7 µg of the placental mRNAs were oxidized as described above in Example 9. The derivatized oligonucleotide was joined to the mRNAs as described in Example 10 above except that the precipitation step was replaced by an exclusion chromatography step to remove derivatized oligodeoxyribonucleotides which were not joined to mRNAs. Exclusion chromatography was performed as follows:

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Ten ml of Ultrogel AcA34 (BioSepra#230151) gel, a mix of agarose and acrylamide, were equilibrated in 50 ml of a solution of 10 mM Tris pH 8.0, 300 mM NaCl, 1 mM EDTA, and 0.05% SDS. The mixture was allowed to sediment. The supernatant was eliminated and the gel was resuspended in 50 ml of buffer. This procedure was repeated 2 or 3 times.

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A glass bead (diameter 3 mm) was introduced into a 2 ml disposable pipette (length 25 cm). The pipette was filled with the gel suspension until the height of the gel stabilized at 1 cm from the top of the pipette. The column was then equilibrated with 20 ml of equilibration buffer (10 mM Tris HCl pH 7.4, 20 mM NaCl).

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Ten  $\mu$ l of the mRNA which had reacted with the derivatized oligonucleotide were mixed in 39  $\mu$ l of 10 mM urea and 2  $\mu$ l of blue-glycerol buffer, which had been prepared by dissolving 5 mg of bromophenol blue in 60% glycerol (v/v), and passing the mixture through a 0.45  $\mu$ m diameter filter.

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The column was then loaded with the mRNAs coupled to the oligonucleotide. As soon as the sample had penetrated, equilibration buffer was added. Hundred  $\mu$ l fractions were then collected. Derivatized oligonucleotide which had not been attached to mRNA appeared in fraction 16 and later fractions. Thus, fractions 3 to 15 were combined and precipitated with ethanol.

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To determine whether the derivatized oligonucleotide was actually linked to mRNA, one tenth of the combined fractions were spotted twice on a nylon membrane and hybridized to a radioactive probe using conventional techniques. The <sup>32</sup>P labeled probe used in these hybridizations was an oligodeoxyribonucleotide of sequence 5'TAATGGTCTCGTGCGAATTCTTGAT3' (SEQ ID NO:4) anticomplementary to the derivatized oligonucleotide. A signal observed after autoradiography, indicated that the derivatized oligonucleotide had been truly joined to the mRNA.

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The remaining nine tenth of the mRNAs which had reacted with the derivatized oligonucleotide was reverse transcribed as follows. A reverse transcription reaction was carried out with reverse transcriptase following the manufacturer's instructions and 50 pmol of nonamers with random sequence as primers.

To ensure that reverse transcription had been carried out through the cap structure, two types of experiments were performed.

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In the first approach, after elimination of RNA of the cDNA:RNA heteroduplexes obtained from the reverse transcription reaction by an alkaline hydrolysis, a portion of the resulting single stranded cDNAs was spotted on a positively charged membrane and hybridized, using conventional methods, to a <sup>32</sup>P labeled probe having a sequence identical to that of the derivatized oligonucleotide. Control spots containing, 1 pmol, 100 fmol, 50 fmol, 10 fmol and 1 fmol of a control oligodeoxyribonucleotide of sequence identical to that of the derivatized oligonucleotide were included. The signal observed in the spots containing the cDNA indicated that approximately 15 fmol of the derivatized oligonucleotide had been reverse transcribed. These results demonstrate that the reverse transcription can be performed through the cap and, in particular, that reverse transcriptase crosses the 5'-P-P-P-5' bond of the cap of eukaryotic messenger RNAs.

In the second type of experiment, the single stranded cDNAs obtained from the above first strand synthesis were used as template for PCR reactions. Two types of reactions were carried out. First, specific amplification of the mRNAs for alpha globin, dehydrogenase, pp15 and elongation factor E4 were carried out using the following pairs of oligodeoxyribonucleotide primers.

#### alpha-globin

GLO-S: 5'CCG ACA AGA CCA ACG TCA AGG CCG C3' (SEQ ID NO:5)
GLO-As: 5'TCA CCA GCA GGC AGT GGC TTA GGA G 3' (SEQ ID NO:6)

#### dehydrogenase

3 DH-S: 5'AGT GAT TCC TGC TAC TTT GGA TGG C3' (SEQ ID NO:7)
3 DH-As: 5'GCT TGG TCT TGT TCT GGA GTT TAG A3' (SEQ ID NO:8)

PP15-S: 5'TCC AGA ATG GGA GAC AAG CCA ATT T3' (SEQ ID NO:9)
PP15-As: 5'AGG GAG GAG GAA ACA GCG TGA GTC C3' (SEQ ID NO:10)

30 Elongation factor E4

pp15

EFAI-S: 5'ATG GGA AAG GAA AAG ACT CAT ATC A3' (SEQ ID NO:11)

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#### EF1A-As: 5'AGC AGC AAC AAT CAG GAC AGC ACA G3' (SEQ ID NO:12)

Second, non specific amplifications were also carried out with the antisense oligodeoxyribonucleotides of the pairs described above and with a primer derived from the sequence of the derivatized oligodeoxyribonucleotide (5'ATCAAGAATTCGCACGAGACCATTA3') (SEQ ID NO:13).

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One twentieth of the following RT-PCR product samples were run on a 1.5% agarose gel and stained with ethidium bromide.

Sample 1: The products of a PCR reaction using the globin primers of SEQ ID NOs 5 and 6 in the presence of cDNA.

Sample 2: The products of a PCR reaction using the globin primers of SEQ ID NOs 5 and 6 in the absence of added cDNA.

Sample 3: The products of a PCR reaction using the dehydrogenase primers of SEQ ID NOs 7 and 8 in the presence of cDNA.

Sample 4: The products of a PCR reaction using the dehydrogenase primers of SEQ ID NOs 7 and 8 in the absence of added cDNA.

Sample 5: The products of a PCR reaction using the pp15 primers of SEQ ID NOs 9 and 10 in the presence of cDNA.

Sample 6: The products of a PCR reaction using the pp15 primers of SEQ ID NOs 9 and 10 in the absence of added cDNA.

Sample 7: The products of a PCR reaction using the EIF4 primers of SEQ ID NOs 11 and 12 in the presence of added cDNA.

Sample 8: The products of a PCR reaction using the EIF4 primers of SEQ ID NOs 11 and 12 in the absence of added cDNA

A band of the size expected for the PCR product was observed only in samples 1, 3, 5 and 7, thus indicating the presence of the corresponding sequence in the cDNA population.

PCR reactions were also carried out with the antisense oligonucleotides of the globin and dehydrogenase primers (SEQ ID NOs 6 and 8) and an oligonucleotide whose sequence corresponds to that of the derivatized oligonucleotide. The presence of PCR products of the expected size in the samples equivalent to above samples 1 and 3 indicated that the derivatized oligonucleotide had been linked to mRNA.

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The above examples summarize the chemical procedure for enriching mRNAs for those having intact 5' ends as illustrated in Figure 1. Further detail regarding the chemical approaches for obtaining such mRNAs are disclosed in International Application No. WO96/34981, published November 7, 1996, which is incorporated herein by reference. Strategies based on the above chemical modifications to the 5' cap structure may be utilized to generate cDNAs selected to include the 5' ends of the mRNAs from which they derived. In one version of such procedures, the 5' ends of the mRNAs are modified as described Thereafter, a reverse transcription reaction is conducted to extend a primer above. complementary to the 5' end of the mRNA. Single stranded RNAs are eliminated to obtain a population of cDNA/mRNA heteroduplexes in which the mRNA includes an intact 5' end. The resulting heteroduplexes may be captured on a solid phase coated with a molecule capable of interacting with the molecule used to derivatize the 5' end of the mRNA. Thereafter, the strands of the heteroduplexes are separated to recover single stranded first cDNA strands which include the 5' end of the mRNA. Second strand cDNA synthesis may then proceed using conventional techniques. For example, the procedures disclosed in WO 96/34981 or in Carninci. et al., Genomics 37:327-336, 1996, the disclosures of which are incorporated herein by reference, may be employed to select cDNAs which include the sequence derived from the 5' end of the coding sequence of the mRNA.

Following ligation of the oligonucleotide tag to the 5' cap of the mRNA, a reverse transcription reaction is conducted to extend a primer complementary to the mRNA to the 5' end of the mRNA. Following elimination of the RNA component of the resulting heteroduplex using standard techniques, second strand cDNA synthesis is conducted with a primer complementary to the oligonucleotide tag.

#### 25 <u>2. Enzymatic Methods for Obtaining mRNAs having Intact 5' Ends</u>

Other techniques for selecting cDNAs extending to the 5' end of the mRNA from which they are derived are fully enzymatic. Some versions of these techniques are disclosed in Dumas Milne Edwards J.B. (Doctoral Thesis of Paris VI University, Le clonage des ADNc complets: difficultes et perspectives nouvelles. Apports pour l'etude de la regulation de l'expression de la tryptophane hydroxylase de rat, 20 Dec. 1993), EP0 625572 and Kato et al., Gene 150:243-250, 1994, the disclosures of which are incorporated herein by reference.

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Briefly, in such approaches, isolated mRNA is treated with alkaline phosphatase to remove the phosphate groups present on the 5' ends of uncapped incomplete mRNAs. Following this procedure, the cap present on full length mRNAs is enzymatically removed with a decapping enzyme such as T4 polynucleotide kinase or tobacco acid pyrophosphatase. An oligonucleotide, which may be either a DNA oligonucleotide or a DNA-RNA hybrid oligonucleotide having RNA at its 3' end, is then ligated to the phosphate present at the 5' end of the decapped mRNA using T4 RNA ligase. The oligonucleotide may include a restriction site to facilitate cloning of the cDNAs following their synthesis. Example 12 below describes one enzymatic method based on the doctoral thesis of Dumas.

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#### **EXAMPLE 12**

#### Enzymatic Approach for Obtaining 5' ESTs

Twenty micrograms of PolyA+ RNA were dephosphorylated using Calf Intestinal Phosphatase (Biolabs). After a phenol chloroform extraction, the cap structure of mRNA was hydrolysed using the Tobacco Acid Pyrophosphatase (purified as described by Shinshi *et al.*., *Biochemistry* 15: 2185-2190, 1976) and a hemi 5'DNA/RNA-3' oligonucleotide having an unphosphorylated 5' end, a stretch of adenosine ribophosphate at the 3' end, and an EcoRI site near the 5' end was ligated to the 5'P ends of mRNA using the T4 RNA ligase (Biolabs). Oligonucleotides suitable for use in this procedure are preferably 30 to 50 bases in length. Oligonucleotides having an unphosphorylated 5' end may be synthesized by adding a fluorochrome at the 5' end. The inclusion of a stretch of adenosine ribophosphates at the 3' end of the oligonucleotide increases ligation efficiency. It will be appreciated that the oligonucleotide may contain cloning sites other than EcoRI.

Following ligation of the oligonucleotide to the phosphate present at the 5' end of the decapped mRNA, first and second strand cDNA synthesis is carried out using conventional methods or those specified in EP0 625,572 and Kato *et al. supra*, and Dumas Milne Edwards, *supra*, the disclosures of which are incorporated herein by reference. The resulting cDNA may then be ligated into vectors such as those disclosed in Kato *et al.*, *supra* or other nucleic acid vectors known to those skilled in the art using techniques such as those described in Sambrook *et al.*, Molecular Cloning: A Laboratory Manual 2d Ed., Cold Spring Harbor Laboratory Press, 1989, the disclosure of which is incorporated herein by reference.

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### II. Obtenti n and Characterization of the 5' ESTs of the Present Invention

The 5' ESTs of the present invention were obtained using the aforementioned chemical and enzymatic approaches for enriching mRNAs for those having intact 5' ends as decribed below.

### 1. Obtention of 5' ESTS Using mRNAs with Intact 5' Ends

First, mRNAs were prepared as described in Example 13 below.

#### **EXAMPLE 13**

### Preparation of mRNA With Intact 5' Ends

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Total human RNAs or polyA<sup>+</sup> RNAs derived from 29 different tissues were respectively purchased from LABIMO and CLONTECH and used to generate 44 cDNA libraries as follows. The purchased RNA had been isolated from cells or tissues using acid guanidium thiocyanate-phenol-chloroform extraction (Chomczyniski and Sacchi, *Analytical Biochemistry* 162:156-159, 1987). PolyA<sup>+</sup> RNA was isolated from total RNA (LABIMO) by two passes of oligo dT chromatography, as described by Aviv and Leder, *Proc. Natl. Acad. Sci. USA* 69:1408-1412, 1972 in order to eliminate ribosomal RNA.

The quality and the integrity of the polyA+ RNAs were checked. Northern blots hybridized with a globin probe were used to confirm that the mRNAs were not degraded. Contamination of the polyA+ mRNAs by ribosomal sequences was checked using Northern blots and a probe derived from the sequence of the 28S rRNA. Preparations of mRNAs with less than 5% of rRNAs were used in library construction. To avoid constructing libraries with RNAs contaminated by exogenous sequences (prokaryotic or fungal), the presence of bacterial 16S ribosomal sequences or of two highly expressed fungal mRNAs was examined using PCR.

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Following preparation of the mRNAs, the above described chemical and/or the enzymatic procedures for enriching mRNAs for thoses having intact 5' ends were employed to obtain 5' ESTs from various tissues. In both approaches, an oligonucleotide tag was attached to the 5' ends of the mRNAs. The oligonucleotide tag had an EcoRI site therein to facilitate later cloning procedures. To facilitate the processing of single stranded and double stranded cDNA obtained in the construction of the librairies, the same nucleotidic sequence

was used to design the ligated oligonucleotide in both chemical and enzymatic approaches. Nevertheless, in the chemical procedure, the tag used was an oligodeoxyribonucleotide which was linked to the cap of the mRNA whereas in the enzymatic ligation, the tag was a chimeric hemi 5'DNA/RNA3' oligonucleotide which was ligated to the 5' end of decapped mRNA as described in example 12.

Following attachment of the oligonucleotide tag to the mRNA by either the chemical or enzymatic methods, the integrity of the mRNA was examined by performing a Northern blot with 200 to 500 ng of mRNA using a probe complementary to the oligonucleotide tag before performing the first strand synthesis as described in example 14.

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#### **EXAMPLE 14**

#### cDNA Synthesis Using mRNA Templates Having Intact 5' Ends

For the mRNAs joined to oligonucleotide tags using both the chemical and enzymatic methods, first strand cDNA synthesis was performed using the Superscript II (Gibco BRL) or the Rnase H Minus M-MLV (Promega) reverse transcriptase with random nonamers as primers. In order to protect internal EcoRI sites in the cDNA from digestion at later steps in the procedure, methylated dCTP was used for first strand synthesis. After removal of RNA by an alkaline hydrolysis, the first strand of cDNA was precipitated using isopropanol in order to eliminate residual primers.

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For both the chemical and the enzymatic methods, the second strand of the cDNA was synthesized with a Klenow fragment using a primer corresponding to the 5' end of the ligated oligonucleotide described in Example 12. Preferably, the primer is 20-25 bases in length. Methylated dCTP was also used for second strand synthesis in order to protect internal EcoRI sites in the cDNA from digestion during the cloning process.

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Following cDNA synthesis, the cDNAs were cloned into pBlueScript as described in Example 15 below.

#### **EXAMPLE 15**

#### Cloning of cDNAsderived from mRNA with intact 5' ends into BlueScript

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Following second strand synthesis, the ends of the cDNA were blunted with T4 DNA polymerase (Biolabs) and the cDNA was digested with EcoRI. Since methylated dCTP was

used during cDNA synthesis, the EcoRI site present in the tag was the only hemi-methylated site, hence the only site susceptible to EcoRI digestion. The cDNA was then size fractionated using exclusion chromatography (AcA, Biosepra) and fractions corresponding to cDNAs of more than 150 bp were pooled and ethanol precipitated. The cDNA was directionally cloned into the SmaI and EcoRI ends of the phagemid pBlueScript vector (Stratagene). The ligation mixture was electroporated into bacteria and propagated under appropriate antibiotic selection.

Clones containing the oligonucleotide tag attached were then selected as described in Example 16 below.

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#### **EXAMPLE 16**

## Selection of Clones Having the Oligonucleotide Tag Attached Thereto

The plasmid DNAs containing 5' EST libraries made as described above were purified (Qiagen). A positive selection of the tagged clones was performed as follows. Briefly, in this selection procedure, the plasmid DNA was converted to single stranded DNA using gene II endonuclease of the phage F1 in combination with an exonuclease (Chang et al., Gene 127:95-8, 1993) such as exonuclease III or T7 gene 6 exonuclease. The resulting single stranded DNA was then purified using paramagnetic beads as described by Fry et al., Biotechniques, 13: 124-131, 1992. In this procedure, the single stranded DNA was hybridized with a biotinylated oligonucleotide having a sequence corresponding to the 3' end of the oligonucleotide described in Example 13. Preferably, the primer has a length of 20-25 bases. Clones including a sequence complementary to the biotinylated oligonucleotide were captured by incubation with streptavidin coated magnetic beads followed by magnetic selection. After capture of the positive clones, the plasmid DNA was released from the magnetic beads and converted into double stranded DNA using a DNA polymerase such as the ThermoSequenase obtained from Amersham Pharmacia Biotech. Alternatively, protocoles such as the one described in the Gene Trapper kit available from Gibco BRL may be used. The double stranded DNA was then electroporated into bacteria. The percentage of positive clones having the 5' tag oligonucleotide was estimated to typically rank between 90 and 98% using dot blot analysis.

Following electroporation, the libraries were ordered in 384-microtiter plates (MTP). A copy of the MTP was stored for future needs. Then the libraries were transferred into 96 MTP and sequenced as described below.

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#### **EXAMPLE 17**

#### Sequencing of Inserts in Selected Clones

Plasmid inserts were first amplified by PCR on PE 9600 thermocyclers (Perkin-Elmer, Applied Biosystems Division, Foster City, CA), using standard SETA-A and SETA-B primers (Genset SA), AmpliTaqGold (Perkin-Elmer), dNTPs (Boehringer), buffer and cycling conditions as recommended by the Perkin-Elmer Corporation.

PCR products were then sequenced using automatic ABI Prism 377 sequencers (Perkin Elmer). Sequencing reactions were performed using PE 9600 thermocyclers with standard dye-primer chemistry and ThermoSequenase (Amersham Pharmacia Biotech). The primers used were either T7 or 21M13 (available from Genset SA) as appropriate. The primers were labeled with the JOE, FAM, ROX and TAMRA dyes. The dNTPs and ddNTPs used in the sequencing reactions were purchased from Boehringer. Sequencing buffer, reagent concentrations and cycling conditions were as recommended by Amersham.

Following the sequencing reaction, the samples were precipitated with ethanol, resuspended in formamide loading buffer, and loaded on a standard 4% acrylamide gel. Electrophoresis was performed for 2.5 hours at 3000V on an ABI 377 sequencer, and the sequence data were collected and analyzed using the ABI Prism DNA Sequencing Analysis Software, version 2.1.2.

# 2. Computer analysis of the Obtained 5' ESTs: Construction of NetGene and SignalTag databases

The sequence data from the 44 cDNA libraries made as described above were transferred to a proprietary database, where quality control and validation steps were performed. A proprietary base-caller, working using a Unix system, automatically flagged suspect peaks, taking into account the shape of the peaks, the inter-peak resolution, and the noise level. The proprietary base-caller also performed an automatic trimming. Any stretch of 25 or fewer bases having more than 4 suspect peaks was considered unreliable and was

discarded. • Sequences corresponding to cloning vector or ligation oligonucleotides were automatically removed from the EST sequences. However, the resulting EST sequences may contain 1 to 5 bases belonging to the above mentioned sequences at their 5' end. If needed, these can easily be removed on a case to case basis.

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Following sequencing as described above, the sequences of the 5' ESTs were entered in NetGene<sup>TM</sup>, a proprietary database called for storage and manipulation as described below. It will be appreciated by those skilled in the art that the data could be stored and manipulated on any medium which can be read and accessed by a computer. Computer readable media include magnetically, optically, or electronically readable media. For example, the computer readable media may be a hard disc, a floppy disc, a magnetic tape, CD-ROM, RAM, or ROM as well as other types of other media known to those skilled in the art.

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In addition, the sequence data may be stored and manipulated in a variety of data processor programs in a diversity of formats. For instance, the sequence data may be stored as text in a word processing file, such as Microsoft WORD or WORDPERFECT or as an ASCII file in a variety of database programs familiar to those of skill in the art, such as DB2, SYBASE, or ORACLE.

The computer readable media on which the sequence information is stored may be in

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a personal computer, a network, a server or other computer systems known to those skilled in the art. The computer or other system preferably includes the storage media described above, and a processor for accessing and manipulating the sequence data. Once the sequence data has been stored, it may be manipulated and searched to locate those stored sequences which contain a desired nucleic acid sequence or which encode a protein having a particular functional domain. For example, the stored sequence information may be compared to other known sequences to identify homologies, motifs implicated in biological function, or structural motifs.

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Programs which may be used to search or compare the stored sequences include the MacPattern (EMBL), BLAST, and BLAST2 program series (NCBI), basic local alignment search tool programs for nucleotide (BLASTN) and peptide (BLASTX) comparisons (Altschul et al, J. Mol. Biol. 215: 403, 1990) and FASTA (Pearson and Lipman, Proc. Natl. Acad. Sci. USA 85: 2444, 1988). The BLAST programs then extend the alignments on the basis of defined match and mismatch criteria.

Motifs which may be detected using the above programs and those described in Example 28 include sequences encoding leucine zippers, helix-turn-helix motifs, glycosylation sites, ubiquitination sites, alpha helices, and beta sheets, signal sequences encoding signal peptides which direct the secretion of the encoded proteins, sequences implicated in transcription regulation such as homeoboxes, acidic stretches, enzymatic active sites, substrate binding sites, and enzymatic cleavage sites.

Before searching the cDNAs in the NetGene<sup>TM</sup> database for sequence motifs of interest, cDNAs derived from mRNAs which were not of interest were identified and eliminated from further consideration as described in Example 18 below.

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#### **EXAMPLE 18**

#### Elimination of Undesired Sequences from Further Consideration

5' ESTs in the NetGene<sup>™</sup> database which were derived from undesired sequences such as transfer RNAs, ribosomal RNAs, mitochondrial RNAs, prokaryotic RNAs, fungal RNAs, Alu sequences, L1 sequences, or repeat sequences were identified using the FASTA and BLASTN programs with the parameters listed in Table I.

To eliminate 5' ESTs encoding tRNAs from further consideration, the 5' EST sequences were compared to the sequences of 1190 known tRNAs obtained from EMBL release 38, of which 100 were human. The comparison was performed using FASTA on both strands of the 5' ESTs. Sequences having more than 80% homology over more than 60 nucleotides were identified as tRNA. Of the 144,341 sequences screened, 26 were identified as tRNAs and eliminated from further consideration.

To eliminate 5' ESTs encoding rRNAs from further consideration, the 5' EST sequences were compared to the sequences of 2497 known rRNAs obtained from EMBL release 38, of which 73 were human. The comparison was performed using BLASTN on both strands of the 5' ESTs with the parameter S=108. Sequences having more than 80% homology over stretches longer than 40 nucleotides were identified as rRNAs. Of the 144,341 sequences screened, 3,312 were identified as rRNAs and eliminated from further consideration.

To eliminate 5' ESTs encoding mtRNAs from further consideration, the 5' EST sequences were compared to the sequences of the two known mitochondrial genomes for

which the entire genomic sequences are available and all sequences transcribed from these mitochondrial genomes including tRNAs, rRNAs, and mRNAs for a total of 38 sequences. The comparison was performed using BLASTN on both strands of the 5' ESTs with the parameter S=108. Sequences having more than 80% homology over stretches longer than 40 nucleotides were identified as mtRNAs. Of the 144,341 sequences screened, 6,110 were identified as mtRNAs and eliminated from further consideration.

Sequences which might have resulted from exogenous contaminants were eliminated from further consideration by comparing the 5' EST sequences to release 46 of the EMBL bacterial and fungal divisions using BLASTN with the parameter S=144. All sequences having more than 90% homology over at least 40 nucleotides were identified as exogenous contaminants. Of the 42 cDNA libraries examined, the average percentages of prokaryotic and fungal sequences contained therein were 0.2% and 0.5% respectively. Among these sequences, only one could be identified as a sequence specific to fungi. The others were either fungal or prokaryotic sequences having homologies with vertebrate sequences or including repeat sequences which had not been masked during the electronic comparison.

In addition, the 5' ESTs were compared to 6093 Alu sequences and 1115 L1 sequences to mask 5' ESTs containing such repeat sequences. 5' ESTs including THE and MER repeats, SSTR sequences or satellite, micro-satellite, or telomeric repeats were also eliminated from further consideration. On average, 11.5% of the sequences in the libraries contained repeat sequences. Of this 11.5%, 7% contained Alu repeats, 3.3% contained L1 repeats and the remaining 1.2% were derived from the other screened types of repetitive sequences. These percentages are consistent with those found in cDNA libraries prepared by other groups. For example, the cDNA libraries of Adams *et al.* contained between 0% and 7.4% Alu repeats depending on the source of the RNA which was used to prepare the cDNA library (Adams *et al.*, *Nature* 377:174, 1996).

The sequences of those 5' ESTs remaining after the elimination of undesirable sequences were compared with the sequences of known human mRNAs to determine the accuracy of the sequencing procedures described above.

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#### **EXAMPLE 19**

# Measurement of Sequencing Accuracy by Comparison to Known Sequences

To further determine the accuracy of the sequencing procedure described above, the sequences of 5' ESTs derived from known sequences were identified and compared to the original known sequences. First, a FASTA analysis with overhangs shorter than 5 bp on both ends was conducted on the 5' ESTs to identify those matching an entry in the public human mRNA database. The 6655 5' ESTs which matched a known human mRNA were then realigned with their cognate mRNA and dynamic programming was used to include substitutions, insertions, and deletions in the list of "errors" which would be recognized. Errors occurring in the last 10 bases of the 5' EST sequences were ignored to avoid the inclusion of spurious cloning sites in the analysis of sequencing accuracy.

This analysis revealed that the sequences incorporated in the NetGene $^{TM}$  database had an accuracy of more than 99.5%.

To determine the efficiency with which the above selection procedures select cDNAs which include the 5' ends of their corresponding mRNAs, the following analysis was performed.

#### **EXAMPLE 20**

## Determination of Efficiency of 5' EST Selection

To determine the efficiency at which the above selection procedures isolated 5' ESTs which included sequences close to the 5' end of the mRNAs from which they derived, the sequences of the ends of the 5' ESTs derived from the elongation factor 1 subunit  $\alpha$  and ferritin heavy chain genes were compared to the known cDNA sequences of these genes. Since the transcription start sites of both genes are well characterized, they may be used to determine the percentage of derived 5' ESTs which included the authentic transcription start sites.

For both genes, more than 95% of the obtained 5' ESTs actually included sequences close to or upstream of the 5' end of the corresponding mRNAs.

To extend the analysis of the reliability of the procedures for isolating 5' ESTs from ESTs in the NetGene<sup>TM</sup> database, a similar analysis was conducted using a database composed of human mRNA sequences extracted from GenBank database release 97 for

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comparison. The 5' ends of more than 85% of 5' ESTs derived from mRNAs included in the GeneBank database were located close to the 5' ends of the known sequence. As some of the mRNA sequences available in the GenBank database are deduced from genomic sequences, a 5' end matching with these sequences will be counted as an internal match. Thus, the method used here underestimates the yield of ESTs including the authentic 5' ends of their corresponding mRNAs.

The EST libraries made above included multiple 5' ESTs derived from the same mRNA. The sequences of such 5' ESTs were compared to one another and the longest 5' ESTs for each mRNA were identified. Overlapping cDNAs were assembled into continuous sequences (contigs). The resulting continuous sequences were then compared to public databases to gauge their similarity to known sequences, as described in Example 21 below.

#### **EXAMPLE 21**

### Clustering of the 5' ESTs and Calculation of Novelty Indices for cDNA Libraries

For each sequenced EST library, the sequences were clustered by the 5' end. Each sequence in the library was compared to the others with BLASTN2 (direct strand, parameters S=107). ESTs with High Scoring Segment Pairs (HSPs) at least 25 bp long, having 95% identical bases and beginning closer than 10 bp from each EST 5' end were grouped. The longest sequence found in the cluster was used as representative of the group. A global clustering between libraries was then performed leading to the definition of super-contigs.

To assess the yield of new sequences within the EST libraries, a novelty rate (NR) was defined as: NR= 100 X (Number of new unique sequences found in the library/Total number of sequences from the library). Typically, novelty rating ranged between 10% and 41% depending on the tissue from which the EST library was obtained. For most of the libraries, the random sequencing of 5' EST libraries was pursued until the novelty rate reached 20%.

Following characterization as described above, the collection of 5' ESTs in NetGene™ was screened to identify those 5' ESTs bearing potential signal sequences as described in Example 22 below.

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#### **EXAMPLE 22**

### Identification of Potential Signal Sequences in 5' ESTs

The 5' ESTs in the NetGene<sup>TM</sup> database were screened to identify those having an uninterrupted open reading frame (ORF) longer than 45 nucleotides beginning with an ATG codon and extending to the end of the EST. Approximately half of the cDNA sequences in NetGene<sup>TM</sup> contained such an ORF. The ORFs of these 5' ESTs were then searched to identify potential signal motifs using slight modifications of the procedures disclosed in Von Heijne, *Nucleic Acids Res.* 14:4683-4690, 1986, the disclosure of which is incorporated herein by reference. Those 5' EST sequences encoding a stretch of at least 15 amino acid long with a score of at least 3.5 in the Von Heijne signal peptide identification matrix were considered to possess a signal sequence. Those 5' ESTs which matched a known human mRNA or EST sequence and had a 5' end more than 20 nucleotides downstream of the known 5' end were excluded from further analysis. The remaining cDNAs having signal sequences therein were included in a database called SignalTag<sup>TM</sup>.

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To confirm the accuracy of the above method for identifying signal sequences, the analysis of Example 23 was performed.

#### **EXAMPLE 23**

20 Confirmation of Accuracy of Identification of Potential Signal Sequences in 5' ESTs

The accuracy of the above procedure for identifying signal sequences encoding signal peptides was evaluated by applying the method to the 43 amino acids located at the N terminus of all human SwissProt proteins. The computed Von Heijne score for each protein was compared with the known characterization of the protein as being a secreted protein or a non-secreted protein. In this manner, the number of non-secreted proteins having a score higher than 3.5 (false positives) and the number of secreted proteins having a score lower than 3.5 (false negatives) could be calculated.

Using the results of the above analysis, the probability that a peptide encoded by the 5' region of the mRNA is in fact a genuine signal peptide based on its Von Heijne's score was calculated based on either the assumption that 10% of human proteins are secreted or the

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assumption that 20% of human proteins are secreted. The results of this analysis are shown in Figure 2 and in Table IV.

Using the above method of identification of secretory proteins, 5' ESTs of the following polypeptides known to be secreted were obtained: human glucagon, gamma interferon induced monokine precursor, secreted cyclophilin-like protein, human pleiotropin, and human biotinidase precursor. Thus, the above method successfully identified those 5' ESTs which encode a signal peptide.

To confirm that the signal peptide encoded by the 5' ESTs actually functions as a signal peptide, the signal sequences from the 5' ESTs may be cloned into a vector designed for the identification of signal peptides. Such vectors are designed to confer the ability to grow in selective medium only to host cells containing a vector with an operably linked signal sequence. For example, to confirm that a 5' EST encodes a genuine signal peptide, the signal sequence of the 5' EST may be inserted upstream and in frame with a non-secreted form of the yeast invertase gene in signal peptide selection vectors such as those described in U.S. Patent No. 5,536,637, the disclosure of which is incorporated herein by reference. Growth of host cells containing signal sequence selection vectors with the correctly inserted 5' EST signal sequence confirms that the 5' EST encodes a genuine signal peptide.

Alternatively, the presence of a signal peptide may be confirmed by cloning the extended cDNAs obtained using the ESTs into expression vectors such as pXT1 (as described below in example 30), or by constructing promoter-signal sequence-reporter gene vectors which encode fusion proteins between the signal peptide and an assayable reporter protein. After introduction of these vectors into a suitable host cell, such as COS cells or NIH 3T3 cells, the growth medium may be harvested and analyzed for the presence of the secreted protein. The medium from these cells is compared to the medium from control cells containing vectors lacking the signal sequence or extended cDNA insert to identify vectors which encode a functional signal peptide or an authentic secreted protein.

Those 5' ESTs which encoded a signal peptide, as determined by the method of Example 22 above, were further grouped into four categories based on their homology to known sequences as described in Example 24 below.

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#### **EXAMPLE 24**

#### Categorization of 5' ESTs Encoding a Signal Peptide

Those 5' ESTs having a sequence not matching any known vertebrate sequence nor any publicly available EST sequence were designated "new." Of the sequences in the SignalTag<sup>TM</sup> database, 947 of the 5' ESTs having a Von Heijne's score of at least 3.5 fell into this category.

Those 5' ESTs having a sequence not matching any vertebrate sequence but matching a publicly known EST were designated "EST-ext", provided that the known EST sequence was extended by at least 40 nucleotides in the 5' direction. Of the sequences in the SignalTag<sup>TM</sup> database, 150 of the 5' ESTs having a Von Heijne's score of at least 3.5 fell into this category.

Those ESTs not matching any vertebrate sequence but matching a publicly known EST without extending the known EST by at least 40 nucleotides in the 5' direction were designated "EST." Of the sequences in the SignalTag<sup>TM</sup> database, 599 of the 5' ESTs having a Von Heijne's score of at least 3.5 fell into this category.

Those 5' ESTs matching a human mRNA sequence but extending the known sequence by at least 40 nucleotides in the 5' direction were designated "VERT-ext." Of the sequences in the SignalTag<sup>TM</sup> database, 23 of the 5' ESTs having a Von Heijne's score of at least 3.5 fell into this category. Included in this category was a 5' EST which extended the known sequence of the human translocase mRNA by more than 200 bases in the 5' direction. A 5' EST which extended the sequence of a human tumor suppressor gene in the 5' direction was also identified.

Table V shows the distribution of 5' ESTs in each category and the number of 5' ESTs in each category having a given minimum von Heijne's score.

3. Evaluation of Spatial and Temporal Expression of mRNAs Corresponding to the 5'ESTs or Extended cDNAs

Each of the 5' ESTs was also categorized based on the tissue from which its corresponding mRNA was obtained, as described below in Example 25.

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#### **EXAMPLE 25**

#### Categorization of Expression Patterns

Table VI shows the distribution of 5' ESTs in each of the above defined category with respect to the tissue from which the 5'ESTs of the corresponding mRNA were obtained.

Table II provides the sequence identification numbers of 5' EST sequences derived from brain, the categories in which these sequences fall, and the von Heijne's score of the signal peptides which they encode. The 5' EST sequences and the amino acid sequences they encode are provided in the appended sequence listings. Table III provides the sequence ID numbers of the 5' ESTs and the sequences of the signal peptides which they encode. The sequences of the 5' ESTs and the polypeptides they encode are provided in the sequence listing appended hereto.

The sequences of DNA SEQ ID NOs: 38-270 can readily be screened for any errors therein and any sequence ambiguities can be resolved by resequencing a fragment containing such errors or ambiguities on both strands. Such fragments may be obtained from the plasmids stored in the inventors' laboratory or can be isolated using the techniques described herein. Resolution of any such ambiguities or errors may be facilitated by using primers which hybridize to sequences located close to the ambiguous or erroneous sequences. For example, the primers may hybridize to sequences within 50-75 bases of the ambiguity or error. Upon resolution of an error or ambiguity, the corresponding corrections can be made in the protein sequences encoded by the DNA containing the error or ambiguity.

In addition to categorizing the 5' ESTs with respect to their tissue of origin, the spatial and temporal expression patterns of the mRNAs corresponding to the 5' ESTs, as well as their expression levels, may be determined as described in Example 26 below. Characterization of the spatial and temporal expression patterns and expression levels of these mRNAs is useful for constructing expression vectors capable of producing a desired level of gene product in a desired spatial or temporal manner, as will be discussed in more detail below.

Furthermore, 5' ESTs whose corresponding mRNAs are associated with disease states may also be identified. For example, a particular disease may result from the lack of expression, over expression, or under expression of an mRNA corresponding to a 5' EST. By comparing mRNA expression patterns and quantities in samples taken from healthy

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individuals with those from individuals suffering from a particular disease, 5' ESTs responsible for the disease may be identified.

It will be appreciated that the results of the above characterization procedures for 5' ESTs also apply to extended cDNAs (obtainable as described below) which contain sequences adjacent to the 5' ESTs. It will also be appreciated that if desired, characterization may be delayed until extended cDNAs have been obtained rather than characterizing the ESTs themselves.

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## Evaluation of Expression Levels and Patterns of mRNAs Corresponding to 5' ESTs or Extended cDNAs

Expression levels and patterns of mRNAs corresponding to 5' ESTs or extended cDNAs (obtainable as described below in example 27) may be analyzed by solution hybridization with long probes as described in International Patent Application No. WO 97/05277, the entire contents of which are hereby incorporated by reference. Briefly, a 5' EST, extended cDNA, or fragment thereof corresponding to the gene encoding the mRNA to be characterized is inserted at a cloning site immediately downstream of a bacteriophage (T3, T7 or SP6) RNA polymerase promoter to produce antisense RNA. Preferably, the 5' EST or extended cDNA has 100 or more nucleotides. The plasmid is linearized and transcribed in the presence of ribonucleotides comprising modified ribonucleotides (i.e. biotin-UTP and DIG-UTP). An excess of this doubly labeled RNA is hybridized in solution with mRNA isolated from cells or tissues of interest. The hybridizations are performed under standard stringent conditions (40-50°C for 16 hours in an 80% formamide, 0.4 M NaCl buffer, pH 7-8). The unhybridized probe is removed by digestion with ribonucleases specific for single-stranded RNA (i.e. RNases CL3, T1, Phy M, U2 or A) The presence of the biotin-UTP modification enables capture of the hybrid on a microtitration plate coated with streptavidin. The presence of the DIG modification enables the hybrid to be detected and quantified by ELISA using an anti-DIG antibody coupled to alkaline phosphatase.

The 5' ESTs, extended cDNAs, or fragments thereof may also be tagged with nucleotide sequences for the serial analysis of gene expression (SAGE) as disclosed in UK

Patent Application No. 2 305 241 A, the entire contents of which are incorporated by reference. In this method, cDNAs are prepared from a cell, tissue, organism or other source of nucleic acid for which gene expression patterns must be determined. The resulting cDNAs are separated into two pools. The cDNAs in each pool are cleaved with a first restriction endonuclease, called an anchoring enzyme, having a recognition site which is likely to be present at least once in most cDNAs. The fragments which contain the 5' or 3' most region of the cleaved cDNA are isolated by binding to a capture medium such as streptavidin coated beads. A first oligonucleotide linker having a first sequence for hybridization of an amplification primer and an internal restriction site for a so-called tagging endonuclease is ligated to the digested cDNAs in the first pool. Digestion with the second endonuclease produces short tag fragments from the cDNAs.

A second oligonucleotide having a second sequence for hybridization of an amplification primer and an internal restriction site is ligated to the digested cDNAs in the second pool. The cDNA fragments in the second pool are also digested with the tagging endonuclease to generate short tag fragments derived from the cDNAs in the second pool. The tags resulting from digestion of the first and second pools with the anchoring enzyme and the tagging endonuclease are ligated to one another to produce so-called ditags. In some embodiments, the ditags are concatamenized to produce ligation products containing from 2 to 200 ditags. The tag sequences are then determined and compared to the sequences of the 5' ESTs or extended cDNAs to determine which 5' ESTs or extended cDNAs are expressed in the cell, tissue, organism, or other source of nucleic acids from which the tags were derived. In this way, the expression pattern of the 5' ESTs or extended cDNAs in the cell, tissue, organism, or other source of nucleic acids is obtained.

Quantitative analysis of gene expression may also be performed using arrays. As used herein, the term array means a one dimensional, two dimensional, or multidimensional arrangement of full length cDNAs (i.e. extended cDNAs which include the coding sequence for the signal peptide, the coding sequence for the mature protein, and a stop codon), extended cDNAs, 5' ESTs or fragments thereof of sufficient length to permit specific detection of gene expression. Preferably, the fragments are at least 15 nucleotides in length. More preferably, the fragments are at least 100 nucleotide long. More preferably, the

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fragments are more than 100 nucleotides in length. In some embodiments, the fragments may be more than 500 nucleotide long.

For example, quantitative analysis of gene expression may be performed with full length cDNAs as defined below, extended cDNAs, 5' ESTs, or fragments thereof in a complementary DNA microarray as described by Schena *et al.* (*Science* 270:467-470, 1995, *Proc. Natl. Acad. Sci. U.S.A.* 93:10614-10619, 1996). Full length cDNAs, extended cDNAs, 5' ESTs or fragments thereof are amplified by PCR and arrayed from 96-well microtiter plates onto silylated microscope slides using high-speed robotics. Printed arrays are incubated in a humid chamber to allow rehydration of the array elements and rinsed, once in 0.2% SDS for 1 min, twice in water for 1 min and once for 5 min in sodium borohydride solution. The arrays are submerged in water for 2 min at 95°C, transferred into 0.2% SDS for 1 min, rinsed twice with water, air dried and stored in the dark at 25°C.

Cell or tissue mRNA is isolated or commercially obtained and probes are prepared by a single round of reverse transcription. Probes are hybridized to 1 cm² microarrays under a 14 x 14 mm glass coverslip for 6-12 hours at 60°C. Arrays are washed for 5 min at 25°C in low stringency wash buffer (1 x SSC/0.2% SDS), then for 10 min at room temperature in high stringency wash buffer (0.1 x SSC/0.2% SDS). Arrays are scanned in 0.1 x SSC using a fluorescence laser scanning device fitted with a custom filter set. Accurate differential expression measurements are obtained by taking the average of the ratios of two independent hybridizations.

Quantitative analysis of the expression of genes may also be performed with full length cDNAs, extended cDNAs, 5' ESTs, or fragments thereof in complementary DNA arrays as described by Pietu et al. (Genome Research 6:492-503, 1996). The full length cDNAs, extended cDNAs, 5' ESTs or fragments thereof are PCR amplified and spotted on membranes. Then, mRNAs originating from various tissues or cells are labeled with radioactive nucleotides. After hybridization and washing in controlled conditions, the hybridized mRNAs are detected by phospho-imaging or autoradiography. Duplicate experiments are performed and a quantitative analysis of differentially expressed mRNAs is then performed.

Alternatively, expression analysis of the 5' ESTs or extended cDNAs can be done through high density nucleotide arrays as described by Lockhart et al. (Nature Biotechnology

14: 1675-1680, 1996) and Sosnowsky et al. (Proc. Natl. Acad. Sci. 94:1119-1123, 1997). Oligonucleotides of 15-50 nucleotides corresponding to sequences of the 5' ESTs or extended cDNAs are synthesized directly on the chip (Lockhart et al., supra) or synthesized and then addressed to the chip (Sosnowsky et al., supra). Preferably, the oligonucleotides are about 20 nucleotides in length.

cDNA probes labeled with an appropriate compound, such as biotin, digoxigenin or fluorescent dye, are synthesized from the appropriate mRNA population and then randomly fragmented to an average size of 50 to 100 nucleotides. The said probes are then hybridized to the chip. After washing as described in Lockhart et al, supra and application of different electric fields (Sonowsky et al, supra.), the dyes or labeling compounds are detected and quantified. Duplicate hybridizations are performed. Comparative analysis of the intensity of the signal originating from cDNA probes on the same target oligonucleotide in different cDNA samples indicates a differential expression of the mRNA corresponding to the 5' EST or extended cDNA from which the oligonucleotide sequence has been designed.

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## III. Use of 5' ESTs to Clone Extended cDNAs and to Clone the Corresponding Genomic DNAs

Once 5' ESTs which include the 5' end of the corresponding mRNAs have been selected using the procedures described above, they can be utilized to isolate extended cDNAs which contain sequences adjacent to the 5' ESTs. The extended cDNAs may include the entire coding sequence of the protein encoded by the corresponding mRNA, including the authentic translation start site, the signal sequence, and the sequence encoding the mature protein remaining after cleavage of the signal peptide. Such extended cDNAs are referred to herein as "full length cDNAs." Alternatively, the extended cDNAs may include only the sequence encoding the mature protein remaining after cleavage of the signal peptide, or only the sequence encoding the signal peptide.

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Example 27 below describes a general method for obtaining extended cDNAs using 5' ESTs. Example 28 below provides experimental results, using the method explained in example 27, describing several extended cDNAs including the entire coding sequence and authentic 5' end of the corresponding mRNA for several secreted proteins.

The methods of Examples 27, 28, and 29 can also be used to obtain extended cDNAs which encode less than the entire coding sequence of the secreted proteins encoded by the genes corresponding to the 5' ESTs. In some embodiments, the extended cDNAs isolated using these methods encode at least 10 amino acids of one of the proteins encoded by the sequences of SEQ ID NOs: 38-270. In further embodiments, the extended cDNAs encode at least 20 amino acids of the proteins encoded by the sequences of SEQ ID NOs: 38-270. In further embodiments, the extended cDNAs encode at least 30 amino amino acids of the sequences of SEQ ID NOs: 38-270. In a preferred embodiment, the extended cDNAs encode a full length protein sequence, which includes the protein coding sequences of SEQ ID NOs: 38-270.

#### **EXAMPLE 27**

### General Method for Using 5' ESTs to Clone and Sequence cDNAs which Include the Entire Coding Region and the Authentic 5' End of the Corresponding mRNA

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The following general method has been used to quickly and efficiently isolate extended cDNAs having the authentic 5' ends of their corresponding mRNAs as well as the full protein coding sequence and including sequence adjacent to the sequences of the 5' ESTs used to obtain them. This method may be applied to obtain extended cDNAs for any 5' EST in the NetGene<sup>TM</sup> database, including those 5' ESTs encoding polypeptides belonging to secreted proteins. The method is summarized in figure 3.

#### 1. Obtention of Extended cDNAs

#### a) First strand synthesis

The method takes advantage of the known 5' sequence of the mRNA. A reverse transcription reaction is conducted on purified mRNA with a poly 14dT primer containing a 49 nucleotide sequence at its 5' end allowing the addition of a known sequence at the end of the cDNA which corresponds to the 3' end of the mRNA. For example, the primer may have the following sequence: 5'-ATC GTT GAG ACT CGT ACC AGC AGA GTC ACG AGA GAG ACT ACA CGG TAC TGG TTT TTT TTT TTT TTT TTVN -3' (SEQ ID NO:14). Those skilled in the art will appreciate that other sequences may also be added to the poly dT sequence and used to prime the first strand synthesis. Using this primer and a reverse

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transcriptase such as the Superscript II (Gibco BRL) or Rnase H Minus M-MLV (Promega) enzyme, a reverse transcript anchored at the 3' polyA site of the RNAs is generated.

After removal of the mRNA hybridized to the first cDNA strand by alkaline hydrolysis, the products of the alkaline hydrolysis and the residual poly dT primer are eliminated with an exclusion column such as an AcA34 (Biosepra) matrix as explained in Example 11.

#### b) Second strand synthesis

A pair of nested primers on each end is designed based on the known 5' sequence from the 5' EST and the known 3' end added by the poly dT primer used in the first strand synthesis. Softwares used to design primers are either based on GC content and melting temperatures of oligonucleotides, such as OSP (Illier and Green, PCR Meth. Appl. 1:124-128, 1991), or based on the octamer frequency disparity method (Griffais et al., Nucleic Acids Res. 19: 3887-3891, 1991) such as PC-Rare (http://bioinformatics.weizmann.ac.il/software/PC-Rare/doc/manuel.html).

Preferably, the nested primers at the 5' end are separated from one another by four to nine bases. The 5' primer sequences may be selected to have melting temperatures and specificities suitable for use in PCR.

Preferably, the nested primers at the 3' end are separated from one another by four to nine bases. For example, the nested 3' primers may have the following sequences: (5'- CCA GCA GAG TCA CGA GAG AGA CTA CAC GG -3'(SEQ ID NO:15), and 5'- CAC GAG AGA GAC TAC ACG GTA CTG G -3' (SEQ ID NO:16). These primers were selected because they have melting temperatures and specificities compatible with their use in PCR. However, those skilled in the art will appreciate that other sequences may also be used as primers.

The first PCR run of 25 cycles is performed using the Advantage Tth Polymerase Mix (Clontech) and the outer primer from each of the nested pairs. A second 20 cycle PCR using the same enzyme and the inner primer from each of the nested pairs is then performed on 1/2500 of the first PCR product. Thereafter, the primers and nucleotides are removed.

#### 2. Sequencing of Full Length Extended cDNAs or Fragments Thereof

Due to the lack of position constraints on the design of 5' nested primers compatible for PCR use using the OSP software, amplicons of two types are obtained. Preferably, the second 5' primer is located upstream of the translation initiation codon thus yielding a nested PCR product containing the whole coding sequence. Such a full length extended cDNA undergoes a direct cloning procedure as described in section a. However, in some cases, the second 5' primer is located downstream of the translation initiation codon, thereby yielding a PCR product containing only part of the ORF. Such incomplete PCR products are submitted to a modified procedure described in section b.

a) Nested PCR products containing complete ORFs

When the resulting nested PCR product contains the complete coding sequence, as predicted from the 5'EST sequence, it is cloned in an appropriate vector such as pED6dpc2, as described in section 3.

#### b) Nested PCR products containing incomplete ORFs

When the amplicon does not contain the complete coding sequence, intermediate steps are necessary to obtain both the complete coding sequence and a PCR product containing the full coding sequence. The complete coding sequence can be assembled.

containing the full coding sequence. The complete coding sequence can be assembled from several partial sequences determined directly from different PCR products as

described in the following section.

Once the full coding sequence has been completely determined, new primers compatible for PCR use are designed to obtain amplicons containing the whole coding region. However, in such cases, 3' primers compatible for PCR use are located inside the 3' UTR of the corresponding mRNA, thus yielding amplicons which lack part of this region, *i.e.* the polyA tract and sometimes the polyadenylation signal, as illustrated in figure 3. Such full length extended cDNAs are then cloned into an appropriate vector as described in section 3.

c) Sequencing extended cDNAs

Sequencing of extended cDNAs is performed using a Die Terminator approach with the AmpliTaq DNA polymerase FS kit available from Perkin Elmer.

In order to sequence PCR fragments, primer walking is performed using software such as OSP to choose primers and automated computer software such as ASMG (Sutton et

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al., Genome Science Technol. 1: 9-19, 1995) to construct contigs of walking sequences including the initial 5' tag using minimum overlaps of 32 nucleotides. Preferably, primer walking is performed until the sequences of full length cDNAs are obtained.

Completion of the sequencing of a given extended cDNA fragment is assessed as follows. Since sequences located after a polyA tract are difficult to determine precisely in the case of uncloned products, sequencing and primer walking processes for PCR products are interrupted when a polyA tract is identified in extended cDNAs obtained as described in case b. The sequence length is compared to the size of the nested PCR product obtained as described above. Due to the limited accuracy of the determination of the PCR product size by gel electrophoresis, a sequence is considered complete if the size of the obtained sequence is at least 70 % the size of the first nested PCR product. If the length of the sequence determined from the computer analysis is not at least 70% of the length of the nested PCR product, these PCR products are cloned and the sequence of the insertion is determined. When Northern blot data are available, the size of the mRNA detected for a given PCR product is used to finally assess that the sequence is complete. Sequences which do not fulfill the above criteria are discarded and will undergo a new isolation procedure.

Sequence data of all extended cDNAs are then transferred to a proprietary database, where quality controls and validation steps are carried out as described in example 15.

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#### 3. Cloning of Full Length Extended cDNAs

The PCR product containing the full coding sequence is then cloned in an appropriate vector. For example, the extended cDNAs can be cloned into the expression vector pED6dpc2 (DiscoverEase, Genetics Institute, Cambridge, MA) as follows. pED6dpc2 vector DNA is prepared with blunt ends by performing an EcoRI digestion followed by a fill in reaction. The blunt ended vector is dephosphorylated. After removal of PCR primers and ethanol precipitation, the PCR product containing the full coding sequence or the extended cDNA obtained as described above is phosphorylated with a kinase subsequently removed by phenol-Sevag extraction and precipitation. The double stranded extended cDNA is then ligated to the vector and the resulting expression plasmid introduced into appropriate host cells.

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Since the PCR products obtained as described above are blunt ended molecules that can be cloned in either direction, the orientation of several clones for each PCR product is determined. Then, 4 to 10 clones are ordered in microtiter plates and subjected to a PCR reaction using a first primer located in the vector close to the cloning site and a second primer located in the portion of the extended cDNA corresponding to the 3' end of the mRNA. This second primer may be the antisense primer used in anchored PCR in the case of direct cloning (case a) or the antisense primer located inside the 3'UTR in the case of indirect cloning (case b). Clones in which the start codon of the extended cDNA is operably linked to the promoter in the vector so as to permit expression of the protein encoded by the extended cDNA are conserved and sequenced. In addition to the ends of cDNA inserts, approximately 50 bp of vector DNA on each side of the cDNA insert are also sequenced.

The cloned PCR products are then entirely sequenced according to the aforementioned procedure. In this case, contigation of long fragments is then performed on walking sequences that have already contigated for uncloned PCR products during primer walking. Sequencing of cloned amplicons is complete when the resulting contigs include the whole coding region as well as overlapping sequences with vector DNA on both ends.

#### 4. Computer analysis of Full Length Extended cDNA

Sequences of all full length extended cDNAs are then submitted to further analysis as described below. Before searching the extended full length cDNAs for sequences of interest, extended cDNAs which are not of interest (vector RNAs, transfer RNAs, ribosomal RNAs, mitochondrial RNAs, prokaryotic RNAs and fungal RNAs) are discarded using methods essentially similar to those described for 5'ESTs in Example 18.

#### a) Identification of structural features

Structural features, e.g. polyA tail and polyadenylation signal, of the sequences of full length extended cDNAs are subsequently determined as follows.

A polyA tail is defined as a homopolymeric stretch of at least 11 A with at most one alternative base within it. The polyA tail search is restricted to the last 100 nt of the sequence and limited to stretches of 11 consecutive A's because sequencing reactions are often not

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readable after such a polyA stretch. Stretches having more than 90% homology over 8 nucleotides are identified as polyA tails using BLAST2N.

To search for a polyadenylation signal, the polyA tail is clipped from the full-length sequence. The 50 bp preceding the polyA tail are first searched for the canonic polyadenylation AAUAAA signal and, if the canonic signal is not detected, for the alternative AUUAAA signal (Sheets et al., Nuc. Acids Res. 18: 5799-5805, 1990). If neither of these consensus polyadenylation signals is found, the canonic motif is searched again allowing one mismatch to account for possible sequencing errors. More than 85 % of identified polyadenylation signals of either type actually ends 10 to 30 bp from the polyA tail. Alternative AUUAAA signals represents approximately 15 % of the total number of identified polyadenylation signals.

#### b) Identification of functional features

Functional features, e.g. ORFs and signal sequences, of the sequences of full length extended cDNAs were subsequently determined as follows.

The 3 upper strand frames of extended cDNAs are searched for ORFs defined as the maximum length fragments beginning with a translation intiation codon and ending with a stop codon. ORFs encoding at least 20 amino acids are preferred.

Each found ORF is then scanned for the presence of a signal peptide in the first 50 amino-acids or, where appropriate, within shorter regions down to 20 amino acids or less in the ORF, using the matrix method of von Heijne (*Nuc. Acids Res.* 14: 4683-4690, 1986), the disclosure of which is incorporated herein by reference as described in Example 22.

### c) Homology to either nucleotidic or proteic sequences

Categorization of full-length sequences may be achieved using procedures essentially similar to those described for 5'ESTs in Example 24.

Extended cDNAs prepared as described above may be subsequently engineered to obtain nucleic acids which include desired portions of the extended cDNA using conventional techniques such as subcloning, PCR, or *in vitro* oligonucleotide synthesis. For example, nucleic acids which include only the full coding sequences (*i.e.* the sequences encoding the signal peptide and the mature protein remaining after the signal peptide is cleaved off) may be

obtained using techniques known to those skilled in the art. Alternatively, conventional techniques may be applied to obtain nucleic acids which contain only the coding sequences for the mature protein remaining after the signal peptide is cleaved off or nucleic acids which contain only the coding sequences for the signal peptides.

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Similarly, nucleic acids containing any other desired portion of the coding sequences for the secreted protein may be obtained. For example, the nucleic acid may contain at least 10 consecutive bases of an extended cDNA such as one of the extended cDNAs described below. In another embodiment, the nucleic acid may contain at least 15 consecutive bases of an extended cDNA such as one of the extended cDNAs described below. Alternatively, the nucleic acid may contain at least 20 consecutive bases of an extended cDNA such as one of the extended cDNAs described below. In another embodiment, the nucleic acid may contain at least 25 consecutive bases of an extended cDNAs uch as one of the extended cDNAs described below. In yet another embodiment, the nucleic acid may contain at least 40 consecutive bases of an extended cDNA such as one of the extended cDNAs described below.

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Once an extended cDNA has been obtained, it can be sequenced to determine the amino acid sequence it encodes. Once the encoded amino acid sequence has been determined, one can create and identify any of the many conceivable cDNAs that will encode that protein by simply using the degeneracy of the genetic code. For example, allelic variants or other homologous nucleic acids can be identified as described below. Alternatively, nucleic acids encoding the desired amino acid sequence can be synthesized *in vitro*.

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In a preferred embodiment, the coding sequence may be selected using the known codon or codon pair preferences for the host organism in which the cDNA is to be expressed.

The extended cDNAs derived from the 5' ESTS of the present invention were obtained as described in Example 28 below.

#### **EXAMPLE 28**

#### Characterization of cloned extended cDNAs obtained using 5' ESTs

The procedure described in Example 27 above was used to obtain the extended cDNAs derived from the 5' ESTs of the present invention in a variety of tissues. The following list provides a few examples of thus obtained extended cDNAs.

Using this approach, the full length cDNA of SEQ ID NO:17 (internal identification number 48-19-3-G1-FL1) was obtained. This cDNA falls into the "EST-ext" category described above and encodes the signal peptide MKKVLLLITAILAVAVG (SEQ ID NO: 18) having a von Heijne score of 8.2.

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The full length cDNA of SEQ ID NO:19 (internal identification number 58-34-2-E7-FL2) was also obtained using this procedure. This cDNA falls into the "EST-ext" category described above and encodes the signal peptide MWWFQQGLSFLPSALVIWTSA (SEQ ID NO:20) having a von Heijne score of 5.5.

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Another full length cDNA obtained using the procedure described above has the sequence of SEQ ID NO:21 (internal identification number 51-27-1-E8-FL1). This cDNA, falls into the "EST-ext" category described above and encodes the signal peptide MVLTTLPSANSANSPVNMPTTGPNSLSYASSALSPCLT (SEQ ID NO:22) having a von Heijne score of 5.9.

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The above procedure was also used to obtain a full length cDNA having the sequence of SEQ ID NO:23 (internal identification number 76-4-1-G5-FL1). This cDNA falls into the "EST-ext" category described above and encodes the signal peptide ILSTVTALTFAXA (SEQ ID NO:24) having a von Heijne score of 5.5.

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The full length cDNA of SEQ ID NO:25 (internal identification number 51-3-3-B10-FL3) was also obtained using this procedure. This cDNA falls into the "new" category described above and encodes a signal peptide LVLTLCTLPLAVA (SEQ ID NO:26) having a von Heijne score of 10.1.

The full length cDNA of SEQ ID NO:27 (internal identification number 58-35-2-F10-FL2) was also obtained using this procedure. This cDNA falls into the "new" category described above and encodes a signal peptide LWLLFFLVTAIHA (SEQ ID NO:28) having a von Heijne score of 10.7.

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Bacterial clones containing plasmids containing the full length cDNAs described above are presently stored in the inventor's laboratories under the internal identification numbers provided above. The inserts may be recovered from the stored materials by growing an aliquot of the appropriate bacterial clone in the appropriate medium. The plasmid DNA can then be isolated using plasmid isolation procedures familiar to those skilled in the art such as alkaline lysis minipreps or large scale alkaline lysis plasmid isolation procedures. If desired

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the plasmid DNA may be further enriched by centrifugation on a cesium chloride gradient, size exclusion chromatography, or anion exchange chromatography. The plasmid DNA obtained using these procedures may then be manipulated using standard cloning techniques familiar to those skilled in the art. Alternatively, a PCR can be done with primers designed at both ends of the cDNA insertion. The PCR product which corresponds to the cDNA can then be manipulated using standard cloning techniques familiar to those skilled in the art.

The polypeptides encoded by the extended cDNAs may be screened for the presence of known structural or functional motifs or for the presence of signatures, small amino acid sequences which are well conserved amongst the members of a protein family. The conserved regions have been used to derive consensus patterns or matrices included in the PROSITE data bank, in particular in the file prosite.dat (Release 13.0 of November 1995, located at <a href="http://expasy.hcuge.ch/sprot/prosite.html">http://expasy.hcuge.ch/sprot/prosite.html</a>. Prosite\_convert and prosite\_scan programs (http://ulrec3.unil.ch/ftpserveur/prosite\_scan) may be used to find signatures on the extended cDNAs.

For each pattern obtained with the prosite\_convert program from the prosite\_dat file, the accuracy of the detection on a new protein sequence may be assessed by evaluating the frequency of irrelevant hits on the population of human secreted proteins included in the data bank SWISSPROT. The ratio between the number of hits on shuffled proteins (with a window size of 20 amino acids) and the number of hits on native (unshuffled) proteins may be used as an index. Every pattern for which the ratio is greater than 20% (one hit on shuffled proteins for 5 hits on native proteins) may be skipped during the search with prosite\_scan. The program used to shuffle protein sequences (db\_shuffled) and the program used to determine the statistics for each pattern in the protein data banks (prosite\_statistics) are available on the ftp site <a href="http://ulrec3 unil ch/ftpserveur/prosite\_scan">https://ulrec3 unil ch/ftpserveur/prosite\_scan</a>.

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In addition to PCR based methods for obtaining extended cDNAs, traditional hybridization based methods may also be employed. These methods may also be used to obtain the genomic DNAs which encode the mRNAs from which the 5' ESTs were derived, mRNAs corresponding to the extended cDNAs, or nucleic acids which are homologous to extended cDNAs or 5' ESTs. Example 29 below provides examples of such methods.

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#### **EXAMPLE 29**

### Methods for Obtaining cDNAs which include the Entire Coding Region and the Authentic 5'End of the Corresponding mRNA

A full length cDNA library can be made using the strategies described in Examples 13, 14, 15, and 16 above by replacing the random nonamer used in Example 14 with an oligodT primer. For instance, the oligonucleotide of SEQ ID NO:14 may be used.

Alternatively, a cDNA library or genomic DNA library may be obtained from a commercial source or made using techniques familiar to those skilled in the art. Such cDNA or genomic DNA librairies may be used to isolate extended cDNAs obtained from 5' EST or nucleic acids homologous to extended cDNAs or 5' EST as follows. The cDNA library or genomic DNA library is hybridized to a detectable probe comprising at least 10 consecutive nucleotides from the 5' EST or extended cDNA using conventional techniques. Preferably, the probe comprises at least 12, 15, or 17 consecutive nucleotides from the 5' EST or extended cDNA. More preferably, the probe comprises at least 20 to 30 consecutive nucleotides from the 5' EST or extended cDNA. In some embodiments, the probe comprises more than 30 nucleotides from the 5' EST or extended cDNA.

Techniques for identifying cDNA clones in a cDNA library which hybridize to a given probe sequence are disclosed in Sambrook et al., Molecular Cloning: A Laboratory Manual 2d Ed., Cold Spring Harbor Laboratory Press, 1989, the disclosure of which is incorporated herein by reference. The same techniques may be used to isolate genomic DNAs.

Briefly, cDNA or genomic DNA clones which hybridize to the detectable probe are identified and isolated for further manipulation as follows. A probe comprising at least 10 consecutive nucleotides from the 5' EST or extended cDNA is labeled with a detectable label such as a radioisotope or a fluorescent molecule. Preferably, the probe comprises at least 12, 15, or 17 consecutive nucleotides from the 5' EST or extended cDNA. More preferably, the probe comprises 20 to 30 consecutive nucleotides from the 5' EST or extended cDNA. In some embodiments, the probe comprises more than 30 nucleotides from the 5' EST or extended cDNA.

Techniques for labeling the probe are well known and include phosphorylation with polynucleotide kinase, nick translation, in vitro transcription, and non radioactive techniques. The cDNAs or genomic DNAs in the library are transferred to a nitrocellulose or nylon filter

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and denatured. After blocking of non specific sites, the filter is incubated with the labeled probe for an amount of time sufficient to allow binding of the probe to cDNAs or genomic DNAs containing a sequence capable of hybridizing thereto.

By varying the stringency of the hybridization conditions used to identify extended cDNAs or genomic DNAs which hybridize to the detectable probe, extended cDNAS having different levels of homology to the probe can be identified and isolated as described below.

### 1. Identification of Extended cDNA or Genomic cDNA Sequences Having a High Degree of Homology to the Labeled Probe

To identify extended cDNAs or genomic DNAs having a high degree of homology to the probe sequence, the melting temperature of the probe may be calculated using the following formulas:

For probes between 14 and 70 nucleotides in length the melting temperature (Tm) is calculated using the formula: Tm=81.5+16.6(log [Na+])+0.41(fraction G+C)-(600/N) where N is the length of the probe.

If the hybridization is carried out in a solution containing formamide, the melting temperature may be calculated using the equation Tm=81.5+16.6(log [Na+])+0.41(fraction G+C)-(0.63% formamide)-(600/N) where N is the length of the probe.

Prehybridization may be carried out in 6X SSC, 5X Denhardt's reagent, 0.5% SDS, 100 µg denatured fragmented salmon sperm DNA or 6X SSC, 5X Denhardt's reagent, 0.5% SDS, 100 µg denatured fragmented salmon sperm DNA, 50% formamide. The formulas for SSC and Denhardt's solutions are listed in Sambrook *et al.*, *supra*.

Hybridization is conducted by adding the detectable probe to the prehybridization solutions listed above. Where the probe comprises double stranded DNA, it is denatured before addition to the hybridization solution. The filter is contacted with the hybridization solution for a sufficient period of time to allow the probe to hybridize to extended cDNAs or genomic DNAs containing sequences complementary thereto or homologous thereto. For probes over 200 nucleotides in length, the hybridization may be carried out at 15-25°C below the Tm. For shorter probes, such as oligonucleotide probes, the hybridization may be conducted at 15-25°C below the Tm. Preferably, for hybridizations in 6X SSC, the

hybridization is conducted at approximately 68°C. Preferably, for hybridizations in 50% formamide containing solutions, the hybridization is conducted at approximately 42°C.

All of the foregoing hybridizations would be considered to be under "stringent" conditions.

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Following hybridization, the filter is washed in 2X SSC, 0.1% SDS at room temperature for 15 minutes. The filter is then washed with 0.1X SSC, 0.5% SDS at room temperature for 30 minutes to 1 hour. Thereafter, the solution is washed at the hybridization temperature in 0.1X SSC, 0.5% SDS. A final wash is conducted in 0.1X SSC at room temperature.

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Extended cDNAs, nucleic acids homologous to extended cDNAs or 5' ESTs, or genomic DNAs which have hybridized to the probe are identified by autoradiography or other conventional techniques.

## 2. Obtention of Extended cDNA or Genomic cDNA Sequences Having Lower Degrees of Homology to the Labeled Probe

The above procedure may be modified to identify extended cDNAs, nucleic acids homologous to extended cDNAs, or genomic DNAs having decreasing levels of homology to the probe sequence. For example, to obtain extended cDNAs, nucleic acids homologous to extended cDNAs, or genomic DNAs of decreasing homology to the detectable probe, less stringent conditions may be used. For example, the hybridization temperature may be decreased in increments of 5°C from 68°C to 42°C in a hybridization buffer having a sodium concentration of approximately 1M. Following hybridization, the filter may be washed with 2X SSC, 0.5% SDS at the temperature of hybridization. These conditions are considered to be "moderate" conditions above 50°C and "low" conditions below 50°C.

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Alternatively, the hybridization may be carried out in buffers, such as 6X SSC, containing formamide at a temperature of 42°C. In this case, the concentration of formamide in the hybridization buffer may be reduced in 5% increments from 50% to 0% to identify clones having decreasing levels of homology to the probe. Following hybridization, the filter may be washed with 6X SSC, 0.5% SDS at 50°C. These conditions are considered to be "moderate" conditions above 25% formamide and "low" conditions below 25% formamide.

Extended cDNAs, nucleic acids homologous to extended cDNAs, or genomic DNAs which have hybridized to the probe are identified by autoradiography.

# 3. Determination of the Degree of Homology Between the Obtained Extended cDNAs and the Labeled Probe

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If it is desired to obtain nucleic acids homologous to extended cDNAs, such as allelic variants thereof or nucleic acids encoding proteins related to the proteins encoded by the extended cDNAs, the level of homology between the hybridized nucleic acid and the extended cDNA or 5' EST used as the probe may be further determined using BLAST2N; parameters may be adapted depending on the sequence length and degree of homology studied. To determine the level of homology between the hybridized nucleic acid and the extended cDNA or 5'EST from which the probe was derived, the nucleotide sequences of the hybridized nucleic acid and the extended cDNA or 5'EST from which the probe was derived are compared. For example, using the above methods, nucleic acids having at least 95% nucleic acid homology to the extended cDNA or 5'EST from which the probe was derived may be obtained and identified. Similarly, by using progressively less stringent hybridization conditions one can obtain and identify nucleic acids having at least 90%, at least 85%, at least 80% or at least 75% homology to the extended cDNA or 5'EST from which the probe was derived.

To determine whether a clone encodes a protein having a given amount of homology to the protein encoded by the extended cDNA or 5' EST, the amino acid sequence encoded by the extended cDNA or 5' EST is compared to the amino acid sequence encoded by the hybridizing nucleic acid. Homology is determined to exist when an amino acid sequence in the extended cDNA or 5' EST is closely related to an amino acid sequence in the hybridizing nucleic acid. A sequence is closely related when it is identical to that of the extended cDNA or 5' EST or when it contains one or more amino acid substitutions therein in which amino acids having similar characteristics have been substituted for one another. Using the above methods and algorithms such as FASTA with parameters depending on the sequence length and degree of homology studied, one can obtain nucleic acids encoding proteins having at least 95%, at least 90%, at least 85%, at least 80% or at least 75% homology to the proteins encoded by the extended cDNA or 5'EST from which the probe was derived.

In addition to the above described methods, other protocols are available to obtain extended cDNAs using 5' ESTs as outlined in the following paragraphs.

Extended cDNAs may be prepared by obtaining mRNA from the tissue, cell, or organism of interest using mRNA preparation procedures utilizing polyA selection procedures or other techniques known to those skilled in the art. A first primer capable of hybridizing to the polyA tail of the mRNA is hybridized to the mRNA and a reverse transcription reaction is performed to generate a first cDNA strand.

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The first cDNA strand is hybridized to a second primer containing at least 10 consecutive nucleotides of the sequences of SEQ ID NOs 38-270. Preferably, the primer comprises at least 12, 15, or 17 consecutive nucleotides from the sequences of SEQ ID NOs 38-270. More preferably, the primer comprises 20 to 30 consecutive nucleotides from the sequences of SEQ ID NOs 38-270. In some embodiments, the primer comprises more than 30 nucleotides from the sequences of SEQ ID NOs 38-270. If it is desired to obtain extended cDNAs containing the full protein coding sequence, including the authentic translation initiation site, the second primer used contains sequences located upstream of the translation initiation site. The second primer is extended to generate a second cDNA strand complementary to the first cDNA strand. Alternatively, RT-PCR may be performed as described above using primers from both ends of the cDNA to be obtained.

Extended cDNAs containing 5' fragments of the mRNA may be prepared by hybridizing an mRNA comprising the sequence of the 5'EST for which an extended cDNA is desired with a primer comprising at least 10 consecutive nucleotides of the sequences complementary to the 5'EST and reverse transcribing the hybridized primer to make a first cDNA strand from the mRNAs. Preferably, the primer comprises at least 12, 15, or 17 consecutive nucleotides from the 5'EST. More preferably, the primer comprises 20 to 30 consecutive nucleotides from the 5'EST.

Thereafter, a second cDNA strand complementary to the first cDNA strand is synthesized. The second cDNA strand may be made by hybridizing a primer complementary to sequences in the first cDNA strand to the first cDNA strand and extending the primer to generate the second cDNA strand.

The double stranded extended cDNAs made using the methods described above are isolated and cloned. The extended cDNAs may be cloned into vectors such as plasmids or

viral vectors capable of replicating in an appropriate host cell. For example, the host cell may be a bacterial, mammalian, avian, or insect cell.

Techniques for isolating mRNA, reverse transcribing a primer hybridized to mRNA to generate a first cDNA strand, extending a primer to make a second cDNA strand complementary to the first cDNA strand, isolating the double stranded cDNA and cloning the double stranded cDNA are well known to those skilled in the art and are described in Current Protocols in Molecular Biology, John Wiley and Sons, Inc. 1997 and Sambrook et al., Molecular Cloning: A Laboratory Manual, Second Edition, Cold Spring Harbor Laboratory Press, 1989, the entire disclosures of which are incorporated herein by reference.

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Alternatively, procedures such as the one described in Example 29 may be used for obtaining full length cDNAs or extended cDNAs. In this approach, full length or extended cDNAs are prepared from mRNA and cloned into double stranded phagemids as follows. The cDNA library in the double stranded phagemids is then rendered single stranded by treatment with an endonuclease, such as the Gene II product of the phage F1, and an exonuclease (Chang et al., Gene 127:95-8, 1993). A biotinylated oligonucleotide comprising the sequence of a 5' EST, or a fragment containing at least 10 nucleotides thereof, is hybridized to the single stranded phagemids. Preferably, the fragment comprises at least 12, 15, or 17 consecutive nucleotides from the 5' EST. More preferably, the fragment comprises 20-30 consecutive nucleotides from the 5' EST. In some procedures, the fragment may comprise more than 30 consecutive nucleotides from the 5' EST.

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Hybrids between the biotinylated oligonucleotide and phagemids having inserts containing the 5' EST sequence are isolated by incubating the hybrids with streptavidin coated paramagnetic beads and retrieving the beads with a magnet (Fry et al., Biotechniques, 13: 124-131, 1992). Therafter, the resulting phagemids containing the 5' EST sequence are released from the beads and converted into double stranded DNA using a primer specific for the 5' EST sequence. Alternatively, protocoles such as the Gene Trapper kit (Gibco BRL) may be used. The resulting double stranded DNA is transformed into bacteria. Extended cDNAs containing the 5' EST sequence are identified by colony PCR or colony hybridization.

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Using any of the above described methods in section III, a plurality of extended cDNAs containing full length protein coding sequences or sequences encoding only the

mature protein remaining after the signal peptide is cleaved off may be provided as cDNA libraries for subsequent evaluation of the encoded proteins or use in diagnostic assays as described below.

### IV. Expression of Proteins Encoded by Extended cDNAs Isolated Using 5' ESTs

Extended cDNAs containing the full protein coding sequences of their corresponding mRNAs or portions thereof, such as cDNAs encoding the mature protein, may be used to express the encoded secreted proteins or portions thereof as described in Example 30 below. If desired, the extended cDNAs may contain the sequences encoding the signal peptide to facilitate secretion of the expressed protein. It will be appreciated that a plurality of extended cDNAs containing the full protein coding sequences or portions thereof may be simultaneously cloned into expression vectors to create an expression library for analysis of the encoded proteins as described below.

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#### **EXAMPLE 30**

## Expression of the Proteins Encoded by the Genes Corresponding to 5'ESTS or Portions Thereof

To express the proteins encoded by the genes corresponding to 5' ESTs (or portions thereof), full length cDNAs containing the entire protein coding region or extended cDNAs containing sequences adjacent to the 5' ESTs (or portions thereof) are obtained as described in Examples 27-29 and cloned into a suitable expression vector. If desired, the nucleic acids may contain the sequences encoding the signal peptide to facilitate secretion of the expressed protein. The nucleic acids inserted into the expression vectors may also contain sequences upstream of the sequences encoding the signal peptide, such as sequences which regulate expression levels or sequences which confer tissue specific expression.

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The nucleic acid encoding the protein or polypeptide to be expressed is operably linked to a promoter in an expression vector using conventional cloning technology. The expression vector may be any of the mammalian, yeast, insect or bacterial expression systems known in the art. Commercially available vectors and expression systems are available from a variety of suppliers including Genetics Institute (Cambridge, MA), Stratagene (La Jolla, California), Promega (Madison, Wisconsin), and Invitrogen (San Diego, California). If desired, to enhance expression and facilitate proper protein folding, the codon context and

codon pairing of the sequence may be optimized for the particular expression organism in which the expression vector is introduced, as explained by Hatfield, *et al.*, U.S. Patent No. 5,082,767, incorporated herein by this reference.

The cDNA cloned into the expression vector may encode the entire protein (*i.e.* the signal peptide and the mature protein), the mature protein (*i.e.* the protein created by cleaving the signal peptide off), only the signal peptide or any other portion thereof.

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The following is provided as one exemplary method to express the proteins encoded by the extended cDNAs corresponding to the 5' ESTs or the nucleic acids described above. First, the methionine initiation codon for the gene and the polyA signal of the gene are identified. If the nucleic acid encoding the polypeptide to be expressed lacks a methionine to serve as the initiation site, an initiating methionine can be introduced next to the first codon of the nucleic acid using conventional techniques. Similarly, if the extended cDNA lacks a polyA signal, this sequence can be added to the construct by, for example, splicing out the polyA signal from pSG5 (Stratagene) using BgIII and SalI restriction endonuclease enzymes and incorporating it into the mammalian expression vector pXT1 (Stratagene). pXT1 contains the LTRs and a portion of the gag gene from Moloney Murine Leukemia Virus. The position of the LTRs in the construct allow efficient stable transfection. The vector includes the Herpes Simplex thymidine kinase promoter and the selectable neomycin gene. The extended cDNA or portion thereof encoding the polypeptide to be expressed is obtained by PCR from the bacterial vector using oligonucleotide primers complementary to the extended cDNA or portion thereof and containing restriction endonuclease sequences for Pst I incorporated into the 5'primer and BglII at the 5' end of the corresponding cDNA 3' primer, taking care to ensure that the extended cDNA is positioned with the poly A signal. The purified fragment obtained from the resulting PCR reaction is digested with PstI, blunt ended with an exonuclease, digested with Bgl II, purified and ligated to pXT1 containing a poly A signal and prepared for this ligation (blunt/BgIII).

The ligated product is transfected into mouse NIH 3T3 cells using Lipofectin (Life Technologies, Inc., Grand Island, New York) under conditions outlined in the product specification. Positive transfectants are selected after growing the transfected cells in 600  $\mu g/ml$  G418 (Sigma, St. Louis, Missouri). Preferably the expressed protein is released into the culture medium, thereby facilitating purification.

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Alternatively, the extended cDNAs may be cloned into pED6dpc2 as described above. The resulting pED6dpc2 constructs may be transfected into a suitable host cell, such as COS 1 cells. Methotrexate resistant cells are selected and expanded. Preferably, the protein expressed from the extended cDNA is released into the culture medium thereby facilitating purification.

Proteins in the culture medium are separated by gel electrophoresis. If desired, the proteins may be ammonium sulfate precipitated or separated based on size or charge prior to electrophoresis.

As a control, the expression vector lacking a cDNA insert is introduced into host cells or organisms and the proteins in the medium are harvested. The secreted proteins present in the medium are detected using techniques familiar to those skilled in the art such as Coomassie blue or silver staining or using antibodies against the protein encoded by the extended cDNA

Antibodies capable of specifically recognizing the protein of interest may be generated using synthetic 15-mer peptides having a sequence encoded by the appropriate 5' EST, extended cDNA, or portion thereof. The synthetic peptides are injected into mice to generate antibody to the polypeptide encoded by the 5' EST, extended cDNA, or portion thereof.

Secreted proteins from the host cells or organisms containing an expression vector which contains the extended cDNA derived from a 5' EST or a portion thereof are compared to those from the control cells or organism. The presence of a band in the medium from the cells containing the expression vector which is absent in the medium from the control cells indicates that the extended cDNA encodes a secreted protein. Generally, the band corresponding to the protein encoded by the extended cDNA will have a mobility near that expected based on the number of amino acids in the open reading frame of the extended cDNA. However, the band may have a mobility different than that expected as a result of modifications such as glycosylation, ubiquitination, or enzymatic cleavage.

Alternatively, if the protein expressed from the above expression vectors does not contain sequences directing its secretion, the proteins expressed from host cells containing an expression vector with an insert encoding a secreted protein or portion thereof can be compared to the proteins expressed in control host cells containing the expression vector without an insert. The presence of a band in samples from cells containing the expression

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vector with an insert which is absent in samples from cells containing the expression vector without an insert indicates that the desired protein or portion thereof is being expressed. Generally, the band will have the mobility expected for the secreted protein or portion thereof. However, the band may have a mobility different than that expected as a result of modifications such as glycosylation, ubiquitination, or enzymatic cleavage.

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The protein encoded by the extended cDNA may be purified using standard immunochromatography techniques. In such procedures, a solution containing the secreted protein, such as the culture medium or a cell extract, is applied to a column having antibodies against the secreted protein attached to the chromatography matrix. The secreted protein is allowed to bind the immunochromatography column. Thereafter, the column is washed to remove non-specifically bound proteins. The specifically bound secreted protein is then released from the column and recovered using standard techniques.

If antibody production is not possible, the extended cDNA sequence or portion thereof may be incorporated into expression vectors designed for use in purification schemes employing chimeric polypeptides. In such strategies, the coding sequence of the extended cDNA or portion thereof is inserted in frame with the gene encoding the other half of the chimera. The other half of the chimera may be  $\beta$ -globin or a nickel binding polypeptide. A chromatography matrix having antibody to  $\beta$ -globin or nickel attached thereto is then used to purify the chimeric protein. Protease cleavage sites may be engineered between the  $\beta$ -globin gene or the nickel binding polypeptide and the extended cDNA or portion thereof. Thus, the two polypeptides of the chimera may be separated from one another by protease digestion.

One useful expression vector for generating β-globin chimerics is pSG5 (Stratagene), which encodes rabbit β-globin. Intron II of the rabbit β-globin gene facilitates splicing of the expressed transcript, and the polyadenylation signal incorporated into the construct increases the level of expression. These techniques as described are well known to those skilled in the art of molecular biology. Standard methods are published in methods texts such as Davis *et al.*, (*Basic Methods in Molecular Biology*, Davis, Dibner, and Battey, ed., Elsevier Press, NY, 1986) and many of the methods are available from Stratagene, Life Technologies, Inc., or Promega. Polypeptide may additionally be produced from the construct using *in vitro* translation systems such as the *In vitro* Express<sup>TM</sup> Translation Kit (Stratagene).

Following expression and purification of the secreted proteins encoded by the 5' ESTs, extended cDNAs, or fragments thereof, the purified proteins may be tested for the ability to bind to the surface of various cell types as described in Example 31 below. It will be appreciated that a plurality of proteins expressed from these cDNAs may be included in a panel of proteins to be simultaneously evaluated for the activities specifically described below, as well as other biological roles for which assays for determining activity are available.

#### **EXAMPLE 31**

### Analysis of Secreted Proteins to Determine Whether they Bind to the Cell Surface

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The proteins encoded by the 5' ESTs, extended cDNAs, or fragments thereof are cloned into expression vectors such as those described in Example 30. The proteins are purified by size, charge, immunochromatography or other techniques familiar to those skilled in the art. Following purification, the proteins are labeled using techniques known to those skilled in the art. The labeled proteins are incubated with cells or cell lines derived from a variety of organs or tissues to allow the proteins to bind to any receptor present on the cell surface. Following the incubation, the cells are washed to remove non-specifically bound protein. The labeled proteins are detected by autoradiography. Alternatively, unlabeled proteins may be incubated with the cells and detected with antibodies having a detectable label, such as a fluorescent molecule, attached thereto.

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Specificity of cell surface binding may be analyzed by conducting a competition analysis in which various amounts of unlabeled protein are incubated along with the labeled protein. The amount of labeled protein bound to the cell surface decreases as the amount of competitive unlabeled protein increases. As a control, various amounts of an unlabeled protein unrelated to the labeled protein is included in some binding reactions. The amount of labeled protein bound to the cell surface does not decrease in binding reactions containing increasing amounts of unrelated unlabeled protein, indicating that the protein encoded by the cDNA binds specifically to the cell surface.

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As discussed above, secreted proteins have been shown to have a number of important physiological effects and, consequently, represent a valuable therapeutic resource. The secreted proteins encoded by the extended cDNAs or portions thereof made according to

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Examples 27-29 may be evaluated to determine their physiological activities as described below.

#### **EXAMPLE 32**

# Assaying the Proteins Expressed from Extended cDNAs or Portions Thereof for Cytokine, Cell Proliferation or Cell Differentiation Activity

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As discussed above, secreted proteins may act as cytokines or may affect cellular proliferation or differentiation. Many protein factors discovered to date, including all known cytokines, have exhibited activity in one or more factor dependent cell proliferation assays, and hence the assays serve as a convenient confirmation of cytokine activity. The activity of a protein encoded by the extended cDNAs is evidenced by any one of a number of routine factor dependent cell proliferation assays for cell lines including, without limitation, 32D, DA2, DA1G, T10, B9, B9/11, BaF3, MC9/G, M (preB M), 2E8, RB5, DA1, 123, T1165, HT2, CTLL2, TF-1, Mo7c and CMK. The proteins encoded by the above extended cDNAs or portions thereof may be evaluated for their ability to regulate T cell or thymocyte proliferation in assays such as those described above or in the following references, which are incorporated herein by reference: Current Protocols in Immunology, Ed. by Coligan et al., Greene Publishing Associates and Wiley-Interscience; Takai et al. J. Immunol. 137:3494-3500, 1986., Bertagnolli et al., J. Immunol. 145:1706-1712, 1990., Bertagnolli et al., Cell. Immunol. 133:327-341, 1991; Bertagnolli, et al., J. Immunol. 149:3778-3783, 1992, Bowman et al., J. Immunol. 152:1756-1761, 1994.

In addition, numerous assays for cytokine production and/or the proliferation of spleen cells, lymph node cells and thymocytes are known. These include the techniques disclosed in *Current Protocols in Immunology*, supra 1:3.12.1-3.12.14; and Schreiber In *Current Protocols in Immunology*, supra 1:6.8.1-6.8.8.

The proteins encoded by the cDNAs may also be assayed for the ability to regulate the proliferation and differentiation of hematopoietic or lymphopoietic cells. Many assays for such activity are familiar to those skilled in the art, including the assays in the following references, which are incorporated herein by reference: Bottomly et al., In Current Protocols in Immunology., supra. 1: 6.3.1-6.3.12,; deVries et al., J. Exp. Med. 173:1205-1211, 1991; Moreau et al., Nature 36:690-692, 1988; Greenberger et al., Proc. Natl. Acad. Sci. U.S.A.

80:2931-2938, 1983; Nordan, R., In Current Protocols in Immunology., supra. 1:6.6.1-6.6.5; Smith et al., Proc. Natl. Acad. Sci. U.S.A. 83:1857-1861, 1986; Bennett et al., in Current Protocols in Immunology supra 1:6.15.1; Ciarletta et al., In Current Protocols in Immunology, supra 1:6.13.1.

The proteins encoded by the cDNAs may also be assayed for their ability to regulate T-cell responses to antigens. Many assays for such activity are familiar to those skilled in the art, including the assays described in the following references, which are incorporated herein by reference. Chapter 3 (In Vitro Assays for Mouse Lymphosyte Function). Chapter 6

art, including the assays described in the following references, which are incorporated herein by reference: Chapter 3 (In Vitro Assays for Mouse Lymphocyte Function), Chapter 6 (Cytokines and Their Cellular Receptors) and Chapter 7, (Immunologic Studies in Humans) in Current Protocols in Immunology supra; Weinberger et al., Proc. Natl. Acad. Sci. USA 77:6091-6095, 1980; Weinberger et al., Eur. J. Immun. 11:405-411, 1981; Takai et al., J.

Immunol. 137:3494-3500, 1986; Takai et al., J. Immunol. 140:508-512, 1988.

Those proteins which exhibit cytokine, cell proliferation, or cell differentiation activity may then be formulated as pharmaceuticals and used to treat clinical conditions in which induction of cell proliferation or differentiation is beneficial. Alternatively, as described in more detail below, genes encoding these proteins or nucleic acids regulating the expression of these proteins may be introduced into appropriate host cells to increase or decrease the expression of the proteins as desired.

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#### **EXAMPLE 33**

## Assaying the Proteins Expressed from Extended cDNAs or Portions Thereof for Activity as Immune System Regulators

The proteins encoded by the cDNAs may also be evaluated for their effects as immune regulators. For example, the proteins may be evaluated for their activity to influence thymocyte or splenocyte cytotoxicity. Numerous assays for such activity are familiar to those skilled in the art including the assays described in the following references, which are incorporated herein by reference: Chapter 3 (In Vitro Assays for Mouse Lymphocyte Function 3.1-3.19) and Chapter 7 (Immunologic studies in Humans) in Current Protocols in Immunology, Coligan et al., Eds, Greene Publishing Associates and Wiley-Interscience; Herrmann et al., Proc. Natl. Acad. Sci. USA 78:2488-2492, 1981; Herrmann et al., J.

Immunol. 128:1968-1974, 1982; Handa et al., J. Immunol. 135:1564-1572, 1985; Takai et al., J. Immunol. 137:3494-3500, 1986; Takai et al., J. Immunol. 140:508-512, 1988; Bowman et al., J. Virology 61:1992-1998; Bertagnolli et al., Cell. Immunol. 133:327-341, 1991; Brown et al., J. Immunol. 153:3079-3092, 1994.

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The proteins encoded by the cDNAs may also be evaluated for their effects on T-cell dependent immunoglobulin responses and isotype switching. Numerous assays for such activity are familiar to those skilled in the art, including the assays disclosed in the following references, which are incorporated herein by reference: Maliszewski, *J. Immunol.* 144:3028-3033, 1990; Mond *et al.* in *Current Protocols in Immunology*, 1:3.8.1-3.8.16, *supra*.

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The proteins encoded by the cDNAs may also be evaluated for their effect on immune effector cells, including their effect on Th1 cells and cytotoxic lymphocytes. Numerous assays for such activity are familiar to those skilled in the art, including the assays disclosed in the following references, which are incorporated herein by reference: Chapter 3 (*In Vitro* Assays for Mouse Lymphocyte Function 3.1-3.19) and Chapter 7 (Immunologic Studies in Humans) in *Current Protocols in Immunology, supra*; Takai et al., J. Immunol. 137:3494-3500, 1986; Takai et al., J. Immunol. 140:508-512, 1988; Bertagnolli et al., J. Immunol. 149:3778-3783, 1992.

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The proteins encoded by the cDNAs may also be evaluated for their effect on dendritic cell mediated activation of naive T-cells. Numerous assays for such activity are familiar to those skilled in the art, including the assays disclosed in the following references, which are incorporated herein by reference: Guery et al., J. Immunol. 134:536-544, 1995; Inaba et al., J. Exp. Med. 173:549-559, 1991; Macatonia et al., J. Immunol. 154:5071-5079, 1995; Porgador et al.J. Exp. Med 182:255-260, 1995; Nair et al., J. Virol. 67:4062-4069, 1993; Huang et al., Science 264:961-965, 1994; Macatonia et al.J. Exp. Med 169:1255-1264, 1989; Bhardwaj et al., Journal of Clinical Investigation 94:797-807, 1994; and Inaba et al., J. Exp. Med 172:631-640, 1990.

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The proteins encoded by the cDNAs may also be evaluated for their influence on the lifetime of lymphocytes. Numerous assays for such activity are familiar to those skilled in the art, including the assays disclosed in the following references, which are incorporated herein by reference: Darzynkiewicz et al., Cytometry 13:795-808, 1992; Gorczyca et al., Leukemia 7:659-670, 1993; Gorczyca et al., Cancer Res. 53:1945-1951, 1993; Itoh et al., Cell 66:233-

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243, 1991; Zacharchuk, J. Immunol. 145:4037-4045, 1990; Zamai et al., Cytometry 14:891-897, 1993; Gorczyca et al., Int. J. Oncol. 1:639-648, 1992.

The proteins encoded by the cDNAs may also be evaluated for their influence on early steps of T-cell commitment and development. Numerous assays for such activity are familiar to those skilled in the art, including without limitation the assays disclosed in the following references, which are incorporated herein by references: Antica et al., Blood 84:111-117, 1994; Fine et al., Cell. Immunol. 155:111-122, 1994; Galy et al., Blood 85:2770-2778, 1995; Toki et al., Proc. Nat. Acad Sci. USA 88:7548-7551, 1991.

Those proteins which exhibit activity as immune system regulators activity may then be formulated as pharmaceuticals and used to treat clinical conditions in which regulation of immune activity is beneficial. For example, the protein may be useful in the treatment of various immune deficiencies and disorders (including severe combined immunodeficiency), e.g., in regulating (up or down) growth and proliferation of T and/or B lymphocytes, as well as effecting the cytolytic activity of NK cells and other cell populations. These immune deficiencies may be genetic or be caused by viral (e.g., HIV) as well as bacterial or fungal infections, or may result from autoimmune disorders. More specifically, infectious diseases caused by viral, bacterial, fungal or other infection may be treatable using a protein encoded by extended cDNAs derived from the 5' ESTs of the present invention, including infections by HIV, hepatitis viruses, herpesviruses, mycobacteria, Leishmania spp., plamodium and various fungal infections such as candidiasis. Of course, in this regard, a protein encoded by extended cDNAs derived from the 5' ESTs of the present invention may also be useful where a boost to the immune system generally may be desirable, i.e., in the treatment of cancer.

Alternatively, proteins encoded by extended cDNAs derived from the 5' ESTs of the present invention may be used in treatment of autoimmune disorders including, for example, connective tissue disease, multiple sclerosis, systemic lupus erythematosus, rheumatoid arthritis, autoimmune pulmonary inflammation, Guillain-Barre syndrome, autoimmune 'thyroiditis, insulin dependent diabetes mellitis, myasthenia gravis, graft-versus-host disease and autoimmune inflammatory eye disease. Such a protein encoded by extended cDNAs derived from the 5' ESTs of the present invention may also to be useful in the treatment of allergic reactions and conditions, such as asthma (particularly allergic asthma) or other respiratory problems. Other conditions, in which immune suppression is desired (including,

for example, organ transplantation), may also be treatable using a protein encoded by extended cDNAs derived from the 5' ESTs of the present invention.

Using the proteins of the invention it may also be possible to regulate immune responses either up or down.

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Down regulation may involve inhibiting or blocking an inunune response already in progress or may involve preventing the induction of an immune response. The functions of activated T-cells may be inhibited by suppressing T cell responses or by inducing specific tolerance in T cells, or both. Immunosuppression of T cell responses is generally an active non-antigen-specific process which requires continuous exposure of the T cells to the suppressive agent. Tolerance, which involves inducing non-responsiveness or anergy in T cells, is distinguishable from immunosuppression in that it is generally antigen-specific and persists after the end of exposure to the tolerizing agent. Operationally, tolerance can be demonstrated by the lack of a T cell response upon reexposure to specific antigen in the absence of the tolerizing agent.

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Down regulating or preventing one or more antigen functions (including without limitation B lymphocyte antigen functions, such as, for example, B7 costimulation), e.g., preventing high level lymphokine synthesis by activated T cells, will be useful in situations of tissue, skin and organ transplantation and in graft-versus-host disease (GVHD). For example, blockage of T cell function should result in reduced tissue destruction in tissue transplantation. Typically, in tissue transplants, rejection of the transplant is initiated through its recognition as foreign by T cells, followed by an immune reaction that destroys the transplant. The administration of a molecule which inhibits or blocks interaction of a B7 lymphocyte antigen with its natural ligand(s) on immune cells (such as a soluble, monomeric form of a peptide having B7-2 activity alone or in conjunction with a monomeric form of a peptide having an activity of another B lymphocyte antigen (e.g., B7-1, B7-3) or blocking antibody), prior to transplantation, can lead to the binding of the molecule to the natural ligand(s) on the immune cells without transmitting the corresponding costimulatory signal. Blocking B lymphocyte antigen function in this matter prevents cytokine synthesis by immune cells, such as T cells, and thus acts as an immunosuppressant. Moreover, the lack of costimulation may also be sufficient to anergize the T cells, thereby inducing tolerance in a subject. Induction of long-term tolerance by B lymphocyte antigen-blocking reagents may

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avoid the necessity of repeated administration of these blocking reagents. To achieve sufficient immunosuppression or tolerance in a subject, it may also be necessary to block the function of a combination of B lymphocyte antigens.

The efficacy of particular blocking reagents in preventing organ transplant rejection or GVHD can be assessed using animal models that are predictive of efficacy in humans. Examples of appropriate systems which can be used include allogeneic cardiac grafts in rats and xenogeneic pancreatic islet cell grafts in mice, both of which have been used to examine the immunosuppressive effects of CTLA4Ig fusion proteins *in vivo* as described in Lenschow *et al.*, *Science* 257:789-792, 1992 and Turka *et al.*, *Proc. Natl. Acad. Sci USA*, 89:11102-11105, 1992. In addition, murine models of GVHD (see Paul ed., *Fundamental Immunology*, Raven Press, New York, 1989, pp. 846-847) can be used to determine the effect of blocking B lymphocyte antigen function *in vivo* on the development of that disease.

Blocking antigen function may also be therapeutically useful for treating autoimmune diseases. Many autoimmune disorders are the result of inappropriate activation of T cells that are reactive against self tissue and which promote the production of cytokines and autoantibodies involved in the pathology of the diseases. Preventing the activation of autoreactive T cells may reduce or eliminate disease symptoms. Administration of reagents which block costimulation of T cells by disrupting receptor/ligand interactions of B lymphocyte antigens can be used to inhibit T cell activation and prevent production of autoantibodies or T cell-derived cytokines which potentially involved in the disease process. Additionally, blocking reagents may induce antigen-specific tolerance of autoreactive T cells which could lead to long-term relief from the disease. The efficacy of blocking reagents in preventing or alleviating autoimmune disorders can be determined using a number of well-characterized animal models of human autoimmune diseases. Examples include murine experimental autoimmune encephalitis, systemic lupus erythmatosis in MRL/pr/pr mice or NZB hybrid mice, murine autoimmuno collagen arthritis, diabetes mellitus in OD mice and BB rats, and murine experimental myasthenia gravis (see Paul ed., supra, pp. 840-856).

Upregulation of an antigen function (preferably a B lymphocyte antigen function), as a means of up regulating immune responses, may also be useful in therapy. Upregulation of immune responses may involve either enhancing an existing immune response or eliciting an initial immune response as shown by the following examples. For instance, enhancing an

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immune response through stimulating B lymphocyte antigen function may be useful in cases of viral infection. In addition, systemic viral diseases such as influenza, the common cold, and encephalitis might be alleviated by the administration of stimulatory form of B lymphocyte antigens systemically.

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Alternatively, antiviral immune responses may be enhanced in an infected patient by removing T cells from the patient, costimulating the T cells *in vitro* with viral antigen-pulsed APCs either expressing a peptide encoded by extended cDNAs derived from the 5' ESTs of the present invention or together with a stimulatory form of a soluble peptide encoded by extended cDNAs derived from the 5' ESTs of the present invention and reintroducing the *in vitro* primed T cells into the patient. The infected cells would now be capable of delivering a costimulatory signal to T cells *in vivo*, thereby activating the T cells.

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In another application, upregulation or enhancement of antigen function (preferably B lymphocyte antigen function) may be useful in the induction of tumor immunity. Tumor cells (e.g., sarcoma, melanoma, lymphoma, leukemia, neuroblastoma, carcinoma) transfected with a nucleic acid encoding at least one peptide encoded by extended cDNAs derived from the 5' ESTs of the present invention can be administered to a subject to overcome tumor-specific tolerance in the subject. If desired, the tumor cell can be transfected to express a combination of peptides. For example, tumor cells obtained from a patient can be transfected *ex vivo* with an expression vector directing the expression of a peptide having B7-2-like activity alone, or in conjunction with a peptide having B7-1-like activity and/or B7-3-like activity. The transfected tumor cells are returned to the patient to result in expression of the peptides on the surface of the transfected cell. Alternatively, gene therapy techniques can be used to target a tumor cell for transfection *in vivo*.

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The presence of the peptide encoded by extended cDNAs derived from the 5' ESTs of the present invention having the activity of a B lymphocyte antigen(s) on the surface of the tumor cell provides the necessary costimulation signal to T cells to induce a T cell mediated immune response against the transfected tumor cells. In addition, tumor cells which lack or which fail to reexpress sufficient amounts of MHC class I or MHC class II molecules can be transfected with nucleic acids encoding all or a portion of (e.g., a cytoplasmic-domain truncated portion) of an MHC class I  $\alpha$  chain and  $\beta_2$  microglobulin or an MHC class II  $\alpha$  chain and an MHC class II  $\beta$  chain to thereby express MHC class I or MHC class II proteins

on the cell surface, respectively. Expression of the appropriate MHC class I or class II molecules in conjunction with a peptide having the activity of a B lymphocyte antigen (e.g., B7-1, B7-2, B7-3) induces a T cell mediated immune response against the transfected tumor cell. Optionally, a gene encoding an antisense construct which blocks expression of an MHC class II associated protein, such as the invariant chain, can also be cotransfected with a DNA encoding a peptide having the activity of a B lymphocyte antigen to promote presentation of tumor associated antigens and induce tumor specific immunity. Thus, the induction of a T cell mediated immune response in a human subject may be sufficient to overcome tumor-specific tolerance in the subject. Alternatively, as described in more detail below, genes encoding these immune system regulator proteins or nucleic acids regulating the expression of such proteins may be introduced into appropriate host cells to increase or decrease the expression of the proteins as desired.

#### **EXAMPLE 34**

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## Assaying the Proteins Expressed from Extended cDNAs or Portions Thereof for Hematopoiesis Regulating Activity

The proteins encoded by the extended cDNAs or portions thereof may also be evaluated for their hematopoiesis regulating activity. For example, the effect of the proteins on embryonic stem cell differentiation may be evaluated. Numerous assays for such activity are familiar to those skilled in the art, including the assays disclosed in the following references, which are incorporated herein by reference: Johansson *et al. Cell. Biol.* 15:141-151, 1995; Keller *et al.*, *Mol. Cell. Biol.* 13:473-486, 1993; McClanahan *et al.*, *Blood* 81:2903-2915, 1993.

The proteins encoded by the extended cDNAs or portions thereof may also be evaluated for their influence on the lifetime of stem cells and stem cell differentiation. Numerous assays for such activity are familiar to those skilled in the art, including the assays disclosed in the following references, which are incorporated herein by reference: Freshney, Methylcellulose Colony Forming Assays, in Culture of Hematopoietic Cells., Freshney, et al.. Eds. pp. 265-268, Wiley-Liss, Inc., New York, NY. 1994; Hirayama et al., Proc. Natl. Acad. Sci. USA 89:5907-5911, 1992; McNiece and Briddell, in Culture of Hematopoietic Cells, supra; Neben et al., Exp. Hematol. 22:353-359, 1994; Ploemacher and Cobblestone In

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Culture of Hematopoietic Cells, supral-21, Spooncer et al, in Culture of Hematopoietic Cells, supra 163-179 and Sutherland in Culture of Hematopoietic Cells, supra. 139-162.

Those proteins which exhibit hematopoiesis regulatory activity may then be formulated as pharmaceuticals and used to treat clinical conditions in which regulation of hematopoeisis is beneficial, such as in the treatment of myeloid or lymphoid cell deficiencies. Involvement in regulating hematopoiesis is indicated even by marginal biological activity in support of colony forming cells or of factor-dependent cell lines. For example, proteins supporting the growth and proliferation of erythroid progenitor cells alone or in combination with other cytokines, indicates utility, for example, in treating various anemias or for use in conjunction with irradiation/chemotherapy to stimulate the production of erythroid precursors and/or erythroid cells. Proteins supporting the growth and proliferation of myeloid cells such as granulocytes and monocytes/macrophages (i.e., traditional CSF activity) may be useful, for example, in conjunction with chemotherapy to prevent or treat consequent myelosuppression. Proteins supporting the growth and proliferation of megakaryocytes and consequently of platelets allows prevention or treatment of various platelet disorders such as thrombocytopenia, and generally may be used in place of or complementary to platelet transfusions. Proteins supporting the growth and proliferation of hematopoietic stem cells which are capable of maturing to any and all of the above-mentioned hematopoietic cells may therefore find therapeutic utility in various stem cell disorders (such as those usually treated with transplantion, including, without limitation, aplastic anemia and paroxysmal nocturnal hemoglobinuria), as well as in repopulating the stem cell compartment post irradiation/chemotherapy, either in vivo or ex vivo (i.e., in conjunction with bone marrow transplantation or with peripheral progenitor cell transplantation (homologous or heterologous)) as normal cells or genetically manipulated for gene therapy. Alternatively, as described in more detail below, genes encoding hematopoiesis regulating activity proteins or nucleic acids regulating the expression of such proteins may be introduced into appropriate host cells to increase or decrease the expression of the proteins as desired.

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#### **EXAMPLE 35**

## Assaying the Proteins Expressed from Extended cDNAs or Portions Thereof for Regulation of Tissue Growth

The proteins encoded by the extended cDNAs or portions thereof may also be evaluated for their effect on tissue growth. Numerous assays for such activity are familiar to those skilled in the art, including the assays disclosed in International Patent Publication No. WO95/16035, International Patent Publication No. WO95/05846 and International Patent Publication No. WO91/07491, which are incorporated herein by reference.

Assays for wound healing activity include, without limitation, those described in: Winter, *Epidermal Wound Healing*, pps. 71-112, Maibach and Rovee, eds., Year Book Medical Publishers, Inc., Chicago, as modified by Eaglstein and Mertz, *J. Invest. Dermatol.* 71:382-84, 1978, which are incorporated herein by reference.

Those proteins which are involved in the regulation of tissue growth may then be formulated as pharmaceuticals and used to treat clinical conditions in which regulation of tissue growth is beneficial. For example, a protein encoded by extended cDNAs derived from the 5' ESTs of the present invention also may have utility in compositions used for bone, cartilage, tendon, ligament and/or nerve tissue growth or regeneration, as well as for wound healing and tissue repair and replacement, and in the treatment of burns, incisions and ulcers.

A protein encoded by extended cDNAs derived from the 5' ESTs of the present invention, which induces cartilage and/or bone growth in circumstances where bone is not normally formed, has application in the healing of bone fractures and cartilage damage or defects in humans and other animals. Such a preparation employing a protein of the invention may have prophylactic use in closed as well as open fracture reduction and also in the improved fixation of artificial joints. *De novo* bone synthesis induced by an osteogenic agent contributes to the repair of congenital, trauma induced, or oncologic resection induced craniofacial defects, and also is useful in cosmetic plastic surgery.

A protein of this invention may also be used in the treatment of periodontal disease, and in other tooth repair processes. Such agents may provide an environment to attract bone-forming cells, stimulate growth of bone-forming cells or induce differentiation of bone-forming cell progenitors. A protein of the invention may also be useful in the treatment of osteoporosis or osteoarthritis, such as through stimulation of bone and/or cartilage repair or

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by blocking inflammation or processes of tissue destruction (collagenase activity, osteoclast activity, etc.) mediated by inflammatory processes.

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Another category of tissue regeneration activity that may be attributable to the protein encoded by extended cDNAs derived from the 5' ESTs of the present invention is tendon/ligament formation. A protein encoded by extended cDNAs derived from the 5' ESTs of the present invention, which induces tendon/ligament-like tissue or other tissue formation in circumstances where such tissue is not normally formed, has application in the healing of tendon or ligament tears, deformities and other tendon or ligament defects in humans and other animals. Such a preparation employing a tendon/ligament-like tissue inducing protein may have prophylactic use in preventing damage to tendon or ligament tissue, as well as use in the improved fixation of tendon or ligament to bone or other tissues, and in repairing defects to tendon or ligament tissue. De novo tendon/ligament-like tissue formation induced by a composition encoded by extended cDNAs derived from the 5' ESTs of the present invention contributes to the repair of tendon or ligaments defects of congenital. traumatic or other origin and is also useful in cosmetic plastic surgery for attachment or repair of tendons or ligaments. The compositions encoded by extended cDNAs derived from the 5' ESTs of the present invention may provide an environment to attract tendon- or ligamentforming cells, stimulate growth of tendon- or ligament-forming cells, induce differentiation of progenitors of tendon- or ligament-forming cells, or induce growth of tendon/ligament cells or progenitors ex vivo for return in vivo to effect tissue repair. The compositions of the invention may also be useful in the treatment of tendinitis, carpal tunnel syndrome and other tendon or ligament defects. The compositions may also include an appropriate matrix and/or sequestering agent as a carrier as is well known in the art.

The protein encoded by extended cDNAs derived from the 5' ESTs of the present invention may also be useful for proliferation of neural cells and for regeneration of nerve and brain tissue, i.e., for the treatment of central and peripheral nervous system diseases and neuropathies, as well as mechanical and traumatic disorders, which involve degeneration, death or trauma to neural cells or nerve tissue. More specifically, a protein may be used in the treatment of diseases of the peripheral nervous system, such as peripheral nerve injuries, peripheral neuropathy and localized neuropathies, and central nervous system diseases, such as Alzheimer's, Parkinson's disease, Huntington's disease, amyotrophic lateral sclerosis, and

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Shy-Drager syndrome. Further conditions which may be treated in accordance with the present invention include mechanical and traumatic disorders, such as spinal cord disorders, head trauma and cerebrovascular diseases such as stroke. Peripheral neuropathies resulting from chemotherapy or other medical therapies may also be treatable using a protein of the invention.

Proteins of the invention may also be useful to promote better or faster closure of non-healing wounds, including without limitation pressure ulcers, ulcers associated with vascular insufficiency, surgical and traumatic wounds, and the like.

It is expected that a protein encoded by extended cDNAs derived from the 5' ESTs of the present invention may also exhibit activity for generation or regeneration of other tissues, such as organs (including, for example, pancreas, liver, intestine, kidney, skin, endothelium) muscle (smooth, skeletal or cardiac) and vascular (including vascular endothelium) tissue, or for promoting the growth of cells comprising such tissues. Part of the desired effects may be by inhibition or modulation of fibrotic scarring to allow normal tissue to generate. A protein of the invention may also exhibit angiogenic activity.

A protein encoded by extended cDNAs derived from the 5' ESTs of the present invention may also be useful for gut protection or regeneration and treatment of lung or liver fibrosis, reperfusion injury in various tissues, and conditions resulting from systemic cytokinc damage.

A protein encoded by extended cDNAs derived from the 5' ESTs of the present invention may also be useful for promoting or inhibiting differentiation of tissues described above from precursor tissues or cells; or for inhibiting the growth of tissues described above.

Alternatively, as described in more detail below, genes encoding tissue growth regulating activity proteins or nucleic acids regulating the expression of such proteins may be introduced into appropriate host cells to increase or decrease the expression of the proteins as desired.

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#### **EXAMPLE 36**

## Assaying the Proteins Expressed from Extended cDNAs or Portions Thereof for Regulation of Reproductive Hormones

The proteins encoded by the extended cDNAs or portions thereof may also be evaluated for their ability to regulate reproductive hormones, such as follicle stimulating hormone. Numerous assays for such activity are familiar to those skilled in the art, including the assays disclosed in the following references, which are incorporated herein by reference: Vale et al., Endocrinol. 91:562-572, 1972; Ling et al., Nature 321:779-782, 1986; Vale et al., Nature 321:776-779, 1986; Mason et al., Nature 318:659-663, 1985; Forage et al., Proc. Natl. Acad. Sci. USA 83:3091-3095, 1986, Chapter 6.12 in Current Protocols in Immunology, Coligan et al. Eds. Greene Publishing Associates and Wiley-Intersciece; Taub et al., J. Clin. Invest. 95:1370-1376, 1995; Lind et al., APMIS 103:140-146, 1995; Muller et al., Eur. J. Immunol. 25:1744-1748; Gruber et al., J. Immunol. 152:5860-5867, 1994; Johnston et al., J Immunol. 153:1762-1768, 1994.

Those proteins which exhibit activity as reproductive hormones or regulators of cell movement may then be formulated as pharmaceuticals and used to treat clinical conditions in which regulation of reproductive hormones are beneficial. For example, a protein encoded by extended cDNAs derived from the 5' ESTs of the present invention may also exhibit activinor inhibin-related activities. Inhibins are characterized by their ability to inhibit the release of follicle stimulating hormone (FSH), while activins are characterized by their ability to stimulate the release of FSH. Thus, a protein encoded by extended cDNAs derived from the 5' ESTs of the present invention, alone or in heterodimers with a member of the inhibin  $\alpha$ family, may be useful as a contraceptive based on the ability of inhibins to decrease fertility in female mammals and decrease spermatogenesis in male mammals. Administration of sufficient amounts of other inhibins can induce infertility in these mammals. Alternatively, the protein of the invention, as a homodimer or as a heterodimer with other protein subunits of the inhibin-B group, may be useful as a fertility inducing therapeutic, based upon the ability of activin molecules in stimulating FSH release from cells of the anterior pituitary. See, for example, United States Patent 4,798,885, the disclosure of which is incorporated herein by reference. A protein of the invention may also be useful for advancement of the onset of fertility in sexually immature mammals, so as to increase the lifetime reproductive performance of domestic animals such as cows, sheep and pigs.

Alternatively, as described in more detail below, genes encoding reproductive hormone regulating activity proteins or nucleic acids regulating the expression of such proteins may be introduced into appropriate host cells to increase or decrease the expression of the proteins as desired.

#### **EXAMPLE 37**

#### Assaying the Proteins Expressed from Extended cDNAs or

10 Portions Thereof for Chemotactic/Chemokinetic Activity

The proteins encoded by the extended cDNAs or portions thereof may also be evaluated for chemotactic/chemokinetic activity. For example, a protein encoded by extended cDNAs derived from the 5' ESTs of the present invention may have chemotactic or chemokinetic activity (e.g., act as a chemokine) for mammalian cells, including, for example, monocytes, fibroblasts, neutrophils, T-cells, mast cells, eosinophils, epithelial and/or endothelial cells. Chemotactic and chemokinetic proteins can be used to mobilize or attract a desired cell population to a desired site of action. Chemotactic or chemokinetic proteins provide particular advantages in treatment of wounds and other trauma to tissues, as well as in treatment of localized infections. For example, attraction of lymphocytes, monocytes or neutrophils to tumors or sites of infection may result in improved immune responses against the tumor or infecting agent.

A protein or peptide has chemotactic activity for a particular cell population if it can stimulate, directly or indirectly, the directed orientation or movement of such cell population. Preferably, the protein or peptide has the ability to directly stimulate directed movement of cells. Whether a particular protein has chemotactic activity for a population of cells can be readily determined by employing such protein or peptide in any known assay for cell chemotaxis.

The activity of a protein of the invention may, among other means, be measured by the following methods:

Assays for chemotactic activity (which will identify proteins that induce or prevent chemotaxis) consist of assays that measure the ability of a protein to induce the migration of

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cells across a membrane as well as the ability of a protein to induce the adhesion of one cell population to another cell population. Suitable assays for movement and adhesion include, without limitation, those described in: *Current Protocols in Immunology*, Ed by Coligan, Kruisbeek, Margulies, Shevach and Strober, Pub. Greene Publishing Associates and Wiley-Interscience, Chapter **6.12**: 6.12.1-6.12.28, Taub *et al.*, *J. Clin. Invest.* **95**:1370-1376, 1995; Lind *et al.*, *APMIS* **103**:140-146, 1995; Mueller *et al.*, *Eur. J. Immunol.* **25**:1744-1748; Gruber *et al.*, *J. Immunol.* **152**:5860-5867, 1994; Johnston *et al. J. Immunol.*, **153**:1762-1768, 1994.

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#### Assaying the Proteins Expressed from Extended cDNAs or Portions Thereof for Regulation of Blood Clotting

The proteins encoded by the extended cDNAs or portions thereof may also be evaluated for their effects on blood clotting. Numerous assays for such activity are familiar to those skilled in the art, including the assays disclosed in the following references, which are incorporated herein by reference: Linet et al., J. Clin. Pharmacol. 26:131-140, 1986; Burdick et al., Thrombosis Res. 45:413-419, 1987; Humphrey et al., Fibrinolysis 5:71-79, 1991; Schaub, Prostaglandins 35:467-474, 1988.

Those proteins which are involved in the regulation of blood clotting may then be formulated as pharmaceuticals and used to treat clinical conditions in which regulation of blood clotting is beneficial. For example, a protein of the invention may also exhibit hemostatic or thrombolytic activity. As a result, such a protein is expected to be useful in treatment of various coagulations disorders (including hereditary disorders, such as hemophilias) or to enhance coagulation and other hemostatic events in treating wounds resulting from trauma, surgery or other causes. A protein of the invention may also be useful for dissolving or inhibiting formation of thromboses and for treatment and prevention of conditions resulting therefrom (such as infarction of cardiac and central nervous system vessels (e.g., stroke)). Alternatively, as described in more detail below, genes encoding blood clotting activity proteins or nucleic acids regulating the expression of such proteins may be introduced into appropriate host cells to increase or decrease the expression of the proteins as desired

#### **EXAMPLE 39**

## Assaying the Proteins Expressed from Extended cDNAs or Portions Thereof for Involvement in Receptor/Ligand Interactions

The proteins encoded by the extended cDNAs or a portion thereof may also be evaluated for their involvement in receptor/ligand interactions. Numerous assays for such involvement are familiar to those skilled in the art, including the assays disclosed in the following references, which are incorporated herein by reference: Chapter 7. 7.28.1-7.28.22 in Current Protocols in Immunology, Coligan et al. Eds. Greene Publishing Associates and Wiley-Interscience; Takai et al., Proc. Natl. Acad. Sci. USA 84:6864-6868, 1987; Bierer et al., J. Exp. Med. 168:1145-1156, 1988; Rosenstein et al., J. Exp. Med. 169:149-160, 1989; Stoltenborg et al., J. Immunol. Methods 175:59-68, 1994; Stitt et al., Cell 80:661-670, 1995; Gyuris et al., Cell 75:791-803, 1993.

For example, the proteins encoded by extended cDNAs derived from the 5' ESTs of the present invention may also demonstrate activity as receptors, receptor ligands or inhibitors or agonists of receptor/ligand interactions. Examples of such receptors and ligands include, without limitation, cytokine receptors and their ligands, receptor kinases and their ligands, receptor phosphatases and their ligands, receptors involved in cell-cell interactions and their ligands (including without limitation, cellular adhesion molecules (such as selectins, integrins and their ligands) and receptor/ligand pairs involved in antigen presentation, antigen recognition and development of cellular and humoral immune responses). Receptors and ligands are also useful for screening of potential peptide or small molecule inhibitors of the relevant receptor/ligand interaction. A protein encoded by extended cDNAs derived from the 5' ESTs of the present invention (including, without limitation, fragments of receptors and ligands) may themselves be useful as inhibitors of receptor/ligand interactions. Alternatively, as described in more detail below, genes encoding proteins involved in receptor/ligand interactions or nucleic acids regulating the expression of such proteins may be introduced into appropriate host cells to increase or decrease the expression of the proteins as desired.

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#### **EXAMPLE 40**

## Assaying the Proteins Expressed from Extended cDNAs or Portions Thereof for Anti-Inflammatory Activity

The proteins encoded by the extended cDNAs or a portion thereof may also be evaluated for anti-inflammatory activity. The anti-inflammatory activity may be achieved by providing a stimulus to cells involved in the inflammatory response, by inhibiting or promoting cell-cell interactions (such as, for example, cell adhesion), by inhibiting or promoting chemotaxis of cells involved in the inflammatory process, inhibiting or promoting cell extravasation, or by stimulating or suppressing production of other factors which more directly inhibit or promote an inflammatory response. Proteins exhibiting such activities can be used to treat inflammatory conditions including chronic or acute conditions, including without limitation inflammation associated with infection (such as septic shock, sepsis or systemic inflammatory response syndrome), ischemia-reperfusioninury, endotoxin lethality, arthritis, complement-mediated hyperacute rejection, nephritis, cytokine- or chemokineinduced lung injury, inflammatory bowel disease, Crohn's disease or resulting from over production of cytokines such as TNF or IL-1. Proteins of the invention may also be useful to treat anaphylaxis and hypersensitivity to an antigenic substance or material. Alternatively, as described in more detail below, genes encoding anti-inflammatory activity proteins or nucleic acids regulating the expression of such proteins may be introduced into appropriate host cells to increase or decrease the expression of the proteins as desired.

#### **EXAMPLE 41**

### Assaying the Proteins Expressed from Extended cDNAs or Portions Thereof for Tumor Inhibition Activity

The proteins encoded by the extended cDNAs or a portion thereof may also be evaluated for tumor inhibition activity. In addition to the activities described above for immunological treatment or prevention of tumors, a protein of the invention may exhibit other anti-tumor activities. A protein may inhibit tumor growth directly or indirectly (such as, for example, via ADCC). A protein may exhibit its tumor inhibitory activity by acting on tumor tissue or tumor precursor tissue, by inhibiting formation of tissues necessary to support tumor growth (such as, for example, by inhibiting angiogenesis), by causing production of other

factors, agents or cell types which inhibit tumor growth, or by suppressing, eliminating or inhibiting factors, agents or cell types which promote tumor growth. Alternatively, as described in more detail below, genes tumor inhibition activity proteins or nucleic acids regulating the expression of such proteins may be introduced into appropriate host cells to increase or decrease the expression of the proteins as desired.

A protein of the invention may also exhibit one or more of the following additional activities or effects: inhibiting the growth, infection or function of, or killing, infectious agents, including, without limitation, bacteria, viruses, fungi and other parasites; effecting (suppressing or enhancing) bodily characteristics, including, without limitation, height, weight, hair color, eye color, skin, fat to lean ratio or other tissue pigmentation, or organ or body part size or shape (such as, for example, breast augmentation or diminution, change in bone form or shape); effecting biorhythms or circadian cycles or rhythms; effecting the fertility of male or female subjects; effecting the metabolism, catabolism, anabolism, processing, utilization, storage or elimination of dietary fat, lipid, protein, carbohydrate, vitamins, minerals, cofactors or other nutritional factors or component(s); effecting behavioral characteristics, including, without limitation, appetite, libido, stress, cognition (including cognitive disorders), depression (including depressive disorders) and violent behaviors; providing analgesic effects or other pain reducing effects; promoting differentiation and growth of embryonic stem cells in lineages other than hematopoietic lineages; hormonal or endocrine activity; in the case of enzymes, correcting deficiencies of the enzyme and treating deficiency-related diseases; treatment of hyperproliferative disorders (such as, for example, psoriasis), immunoglobulin-like activity (such as, for example, the ability to bind antigens or complement); and the ability to act as an antigen in a vaccine composition to raise an immune response against such protein or another material or entity which is cross-reactive with such protein. Alternatively, as described in more detail below, genes encoding proteins involved in any of the above mentioned activities or nucleic acids regulating the expression of such proteins may be introduced into appropriate host cells to increase or decrease the expression of the proteins as desired.

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#### **EXAMPLE 42**

# Identification of Proteins which Interact with Polypeptides Encoded by Extended cDNAs

Proteins which interact with the polypeptides encoded by cDNAs derived from the 5' ESTs or fragments thereof, such as receptor proteins, may be identified using two hybrid systems such as the Matchmaker Two Hybrid System 2 (Catalog No. K1604-1, Clontech). As described in the manual accompanying the kit which is incorporated herein by reference, the the cDNAs derived from 5' ESTs, or fragments thereof, are inserted into an expression vector such that they are in frame with DNA encoding the DNA binding domain of the yeast transcriptional activator GAL4. cDNAs in a cDNA library which encode proteins which might interact with the polypeptides encoded by the extended cDNAs or portions thereof are inserted into a second expression vector such that they are in frame with DNA encoding the activation domain of GAL4. The two expression plasmids are transformed into yeast and the yeast are plated on selection medium which selects for expression of selectable markers on each of the expression vectors as well as GAL4 dependent expression of the HIS3 gene. Transformants capable of growing on medium lacking histidine are screened for GAL4 dependent lacZ expression. Those cells which are positive in both the histidine selection and the lacZ assay contain plasmids encoding proteins which interact with the polypeptide encoded by the extended cDNAs or portions thereof.

Alternatively, the system described in Lustig et al., Methods in Enzymology 283: 83-99, 1997, and in U.S. Patent No. 5,654,150, the disclosure of which is incorporated herein by reference, may be used for identifying molecules which interact with the polypeptides encoded by extended cDNAs. In such systems, in vitro transcription reactions are performed on a pool of vectors containing extended cDNA inserts cloned downstream of a promoter which drives in vitro transcription. The resulting pools of mRNAs are introduced into Xenopus laevis oocytes. The oocytes are then assayed for a desired activity.

Alternatively, the pooled *in vitro* transcription products produced as described above may be translated *in vitro*. The pooled *in vitro* translation products can be assayed for a desired activity or for interaction with a known polypeptide.

Proteins or other molecules interacting with polypeptides encoded by extended cDNAs can be found by a variety of additional techniques. In one method, affinity

columns containing the polypeptide encoded by the extended cDNA or a portion thereof can be constructed. In some versions, of this method the affinity column contains chimeric proteins in which the protein encoded by the extended cDNA or a portion thereof is fused to glutathione S-transferase. A mixture of cellular proteins or pool of expressed proteins as described above and is applied to the affinity column. Proteins interacting with the polypeptide attached to the column can then be isolated and analyzed on 2-D electrophoresis gel as described in Ramunsen et al., Electrophoresis 18:588-598, 1997, the disclosure of which is incorporated herein by reference. Alternatively, the proteins retained on the affinity column can be purified by electrophoresis based methods and sequenced. The same method can be used to isolate antibodies, to screen phage display products, or to screen phage display human antibodies.

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Proteins interacting with polypeptides encoded by extended cDNAs or portions thereof can also be screened by using an Optical Biosensor as described in Edwards and Leatherbarrow, Analytical Biochemistry 246:1-6, 1997, the disclosure of which is incorporated herein by reference. The main advantage of the method is that it allows the determination of the association rate between the protein and other interacting molecules. Thus, it is possible to specifically select interacting molecules with a high or low association rate. Typically a target molecule is linked to the sensor surface (through a carboxymethl dextran matrix) and a sample of test molecules is placed in contact with the target molecules. The binding of a test molecule to the target molecule causes a change in the refractive index and/ or thickness. This change is detected by the Biosensor provided it occurs in the evanescent field (which extend a few hundred nanometers from the sensor surface). In these screening assays, the target molecule can be one of the polypeptides encoded by extended cDNAs or a portion thereof and the test sample can be a collection of proteins extracted from tissues or cells, a pool of expressed proteins, combinatorial peptide and/ or chemical libraries, or phage displayed peptides. The tissues or cells from which the test proteins are extracted can originate from any species.

In other methods, a target protein is immobilized and the test population is a collection of unique polypeptides encoded by the extended cDNAs or portions thereof.

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To study the interaction of the proteins encoded by the extended cDNAs or portions thereof with drugs, the microdialysis coupled to HPLC method described by Wang et al., Chromatographia 44:205-208, 1997 or the affinity capillary electrophoresis method described by Busch et al., J. Chromatogr. 777:311-328, 1997, the disclosures of which are incorporated herein by reference can be used.

It will be appreciated by those skilled in the art that the proteins expressed from the extended cDNAs or portions may be assayed for numerous activities in addition to those specifically enumerated above. For example, the expressed proteins may be evaluated for applications involving control and regulation of inflammation, tumor proliferation or metastasis, infection, or other clinical conditions. In addition, the proteins expressed from the extended cDNAs or portions thereof may be useful as nutritional agents or cosmetic agents.

The proteins expressed from the cDNAs or portions thereof may be used to generate antibodies capable of specifically binding to the expressed protein or fragments thereof as described in Example 40 below. The antibodies may capable of binding a full length protein encoded by a cDNA derived from a 5' EST, a mature protein (*i.e.* the protein generated by cleavage of the signal peptide) encoded by a cDNA derived from a 5' EST. Alternatively, the antibodies may be capable of binding fragments of at least 10 amino acids of the proteins encoded by the above cDNAs. In some embodiments, the antibodies may be capable of binding fragments of at least 15 amino acids of the proteins encoded by the above cDNAs. In other embodiments, the antibodies may be capable of binding fragments of at least 25 amino acids of the proteins expressed from the extended cDNAs which comprise at least 25 amino acids of the proteins encoded by the above cDNAs. In further embodiments, the antibodies may be capable of binding fragments of at least 25 amino acids of the proteins encoded by the above cDNAs. In further embodiments, the antibodies may be capable of binding fragments of at least 40 amino acids of the proteins encoded by the above cDNAs.

#### **EXAMPLE 43**

### Production of an Antibody to a Human Protein

Substantially pure protein or polypeptide is isolated from the transfected or transformed cells as described in Example 30. The concentration of protein in the final preparation is adjusted, for example, by concentration on an Amicon filter device, to the

level of a few µg/ml. Monoclonal or polyclonal antibody to the protein can then be prepared as follows:

#### 1. Monoclonal Antibody Production by Hybridoma Fusion

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Monoclonal antibody to epitopes of any of the peptides identified and isolated as described can be prepared from murine hybridomas according to the classical method of Kohler, and Milstein, Nature 256:495, 1975 or derivative methods thereof. Briefly, a mouse is repetitively inoculated with a few micrograms of the selected protein or peptides derived therefrom over a period of a few weeks. The mouse is then sacrificed, and the antibody producing cells of the spleen isolated. The spleen cells are fused by means of polyethylene glycol with mouse myeloma cells, and the excess unfused cells destroyed by growth of the system on selective media comprising aminopterin (HAT media). The successfully fused cells are diluted and aliquots of the dilution placed in wells of a microtiter plate where growth of the culture is continued. Antibody-producing clones are identified by detection of antibody in the supernatant fluid of the wells by immunoassay procedures, such as ELISA, as originally described by Engvall, Meth. Enzymol. 70:419, 1980, the disclosure of which is incorporated herein by reference and derivative methods thereof. Selected positive clones can be expanded and their monoclonal antibody product harvested for use. Detailed procedures for monoclonal antibody production are described in Davis et al. in Basic Methods in Molecular Biology Elsevier, New York. Section 21-2, the disclosure of which is incorporated herein by reference.

2. Polyclonal Antibody Production by Immunization

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Polyclonal antiserum containing antibodies to heterogenous epitopes of a single protein can be prepared by immunizing suitable animals with the expressed protein or peptides derived therefrom, which can be unmodified or modified to enhance immunogenicity. Effective polyclonal antibody production is affected by many factors related both to the antigen and the host species. For example, small molecules tend to be less immunogenic than others and may require the use of carriers and adjuvant. Also, host animals response vary depending on site of inoculations and doses, with both inadequate or

excessive doses of antigen resulting in low titer antisera. Small doses (ng level) of antigen administered at multiple intradermal sites appears to be most reliable. An effective immunization protocol for rabbits can be found in Vaitukaitis. *et al., J. Clin. Endocrinol. Metab.* 33:988-991 (1971), the disclosure of which is incorporated herein by reference..

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Booster injections can be given at regular intervals, and antiserum harvested when antibody titer thereof, as determined semi-quantitatively, for example, by double immunodiffusion in agar against known concentrations of the antigen, begins to fall. See, for example, Ouchterlony, et al., Chap. 19 in: Handbook of Experimental Immunology D. Wier (ed) Blackwell (1973), the disclosure of which is incorporated herein by reference. Plateau concentration of antibody is usually in the range of 0.1 to 0.2 mg/ml of serum (about 12  $\mu$ M). Affinity of the antisera for the antigen is determined by preparing competitive binding curves, as described, for example, by Fisher, D., Chap. 42 in: Manual of Clinical Immunology, 2d Ed. (Rose and Friedman, Eds.) Amer. Soc. For Microbiol., Washington, D.C. (1980), the disclosure of which is incorporated herein by reference.

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Antibody preparations prepared according to either protocol are useful in quantitative immunoassays which determine concentrations of antigen-bearing substances in biological samples; they are also used semi-quantitatively or qualitatively to identify the presence of antigen in a biological sample. The antibodies may also be used in therapeutic compositions for killing cells expressing the protein or reducing the levels of the protein in the body.

# V. Use of 5' ESTs or Sequences Obtainable Therefrom or Portions Thereof as Reagents

The 5' ESTs of the present invention (or cDNAs or genomic DNAs obtainable therefrom) may be used as reagents in isolation procedures, diagnostic assays, and forensic procedures. For example, sequences from the 5' ESTs (or cDNAs or genomic DNAs obtainable therefrom) may be detectably labeled and used as probes to isolate other sequences capable of hybridizing to them. In addition, sequences from 5' ESTs (or cDNAs or genomic DNAs obtainable therefrom) may be used to design PCR primers to be used in isolation, diagnostic, or forensic procedures.

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## 1. Use of 5' ESTs or Sequences Obtainable Therefrom or Portions Thereof in Isolation, Diagnostic and Forensic Procedures

#### **EXAMPLE 44**

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#### Preparation of PCR Primers and Amplification of DNA

The 5' EST sequences (or cDNAs or genomic DNAs obtainable therefrom) may be used to prepare PCR primers for a variety of applications, including isolation procedures for cloning nucleic acids capable of hybridizing to such sequences, diagnostic techniques and forensic techniques. The PCR primers are at least 10 bases, and preferably at least 12, 15, or 17 bases in length. More preferably, the PCR primers are at least 20-30 bases in length. In some embodiments, the PCR primers may be more than 30 bases in length. It is preferred that the primer pairs have approximately the same G/C ratio, so that melting temperatures are approximately the same. A variety of PCR techniques are familiar to those skilled in the art. For a review of PCR technology, see Molecular Cloning to Genetic Engineering, White Ed. in Methods in Molecular Biology 67: Humana Press, Totowa 1997, the disclosure of which is incorporated herein by reference. In each of these PCR procedures, PCR primers on either side of the nucleic acid sequences to be amplified are added to a suitably prepared nucleic acid sample along with dNTPs and a thermostable polymerase such as Taq polymerase, Pfu polymerase, or Vent polymerase. The nucleic acid in the sample is denatured and the PCR primers are specifically hybridized to complementary nucleic acid sequences in the sample. The hybridized primers are extended. Thereafter, another cycle of denaturation. hybridization, and extension is initiated. The cycles are repeated multiple times to produce an amplified fragment containing the nucleic acid sequence between the primer sites.

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#### **EXAMPLE 45**

#### Use of 5'ESTs as Probes

Probes derived from 5' ESTs (or cDNAs or genomic DNAs obtainable therefrom), including full length cDNAs or genomic sequences, may be labeled with detectable labels familiar to those skilled in the art, including radioisotopes and non-radioactive labels, to provide a detectable probe. The detectable probe may be single stranded or double stranded and may be made using techniques known in the art, including *in vitro* transcription, nick

translation, or kinase reactions. A nucleic acid sample containing a sequence capable of hybridizing to the labeled probe is contacted with the labeled probe. If the nucleic acid in the sample is double stranded, it may be denatured prior to contacting the probe. In some applications, the nucleic acid sample may be immobilized on a surface such as a nitrocellulose or nylon membrane. The nucleic acid sample may comprise nucleic acids obtained from a variety of sources, including genomic DNA, cDNA libraries, RNA, or tissue samples.

Procedures used to detect the presence of nucleic acids capable of hybridizing to the detectable probe include well known techniques such as Southern blotting, Northern blotting, dot blotting, colony hybridization, and plaque hybridization. In some applications, the nucleic acid capable of hybridizing to the labeled probe may be cloned into vectors such as expression vectors, sequencing vectors, or *in vitro* transcription vectors to facilitate the characterization and expression of the hybridizing nucleic acids in the sample. For example, such techniques may be used to isolate and clone sequences in a genomic library or cDNA library which are capable of hybridizing to the detectable probe as described in Example 30 above.

PCR primers made as described in Example 44 above may be used in forensic analyses, such as the DNA fingerprinting techniques described in Examples 46-50 below. Such analyses may utilize detectable probes or primers based on the sequences of the the 5' ESTs or of cDNAs or genomic DNAs isolated using the 5' ESTs.

EXAMPLE 46

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### Forensic Matching by DNA Sequencing

In one exemplary method, DNA samples are isolated from forensic specimens of, for example, hair, semen, blood or skin cells by conventional methods. A panel of PCR primers based on a number of the 5' ESTs of Example 25, or cDNAs or genomic DNAs isolated therefrom as described above, is then utilized in accordance with Example 44 to amplify DNA of approximately 100-200 bases in length from the forensic specimen. Corresponding sequences are obtained from a test subject. Each of these identification DNAs is then sequenced using standard techniques, and a simple database comparison determines the differences, if any, between the sequences from the subject and those from the sample. Statistically significant differences between the suspect's DNA sequences and those from the sample conclusively prove a lack of identity. This lack of identity can be proven, for example,

with only one sequence. Identity, on the other hand, should be demonstrated with a large number of sequences, all matching. Preferably, a minimum of 50 statistically identical sequences of 100 bases in length are used to prove identity between the suspect and the sample.

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#### **EXAMPLE 47**

#### Positive Identification by DNA Sequencing

The technique outlined in the previous example may also be used on a larger scale to provide a unique fingerprint-type identification of any individual. In this technique, primers are prepared from a large number of 5'EST sequences from Example 25, or cDNA or genomic DNA sequences obtainable therefrom. Preferably, 20 to 50 different primers are used. These primers are used to obtain a corresponding number of PCR-generated DNA segments from the individual in question in accordance with Example 44. Each of these DNA segments is sequenced, using the methods set forth in Example 46. The database of sequences generated through this procedure uniquely identifies the individual from whom the sequences were obtained. The same panel of primers may then be used at any later time to absolutely correlate tissue or other biological specimen with that individual.

#### **EXAMPLE 48**

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#### Southern Blot Forensic Identification

The procedure of Example 47 is repeated to obtain a panel of at least 10 amplified sequences from an individual and a specimen. Preferably, the panel contains at least 50 amplified sequences. More preferably, the panel contains 100 amplified sequences. In some embodiments, the panel contains 200 amplified sequences. This PCR-generated DNA is then digested with one or a combination of, preferably, four base specific restriction enzymes. Such enzymes are commercially available and known to those of skill in the art. After digestion, the resultant gene fragments are size separated in multiple duplicate wells on an agarose gel and transferred to nitrocellulose using Southern blotting techniques well known to those with skill in the art. For a review of Southern blotting see Davis *et al.* (Basic Methods in Molecular Biology, 1986, Elsevier Press. pp 62-65), the disclosure of which is incorporated herein by reference.

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A panel of probes based on the sequences of 5' ESTs (or cDNAs or genomic DNAs obtainable therefrom), or fragments thereof of at least 10 bases, are radioactively or colorimetrically labeled using methods known in the art, such as nick translation or end labeling, and hybridized to the Southern blot using techniques known in the art (Davis *et al.*, supra). Preferably, the probe comprises at least 12, 15, or 17 consecutive nucleotides from the 5' EST (or cDNAs or genomic DNAs obtainable therefrom). More preferably, the probe comprises at least 20-30 consecutive nucleotides from the 5' EST (or cDNAs or genomic DNAs obtainable therefrom). In some embodiments, the probe comprises more than 30 nucleotides from the 5' EST (or cDNAs or genomic DNAs obtainable therefrom).

Preferably, at least 5 to 10 of these labeled probes are used, and more preferably at least about 20 or 30 are used to provide a unique pattern. The resultant bands appearing from the hybridization of a large sample of 5' EST (or cDNAs or genomic DNAs obtainable therefrom) will be a unique identifier. Since the restriction enzyme cleavage will be different for every individual, the band pattern on the Southern blot will also be unique. Increasing the number of 5' EST (or cDNAs or genomic DNAs obtainable therefrom) probes will provide a statistically higher level of confidence in the identification since there will be an increased number of sets of bands used for identification.

#### **EXAMPLE 49**

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#### **Dot Blot Identification Procedure**

Another technique for identifying individuals using the 5' EST sequences disclosed herein utilizes a dot blot hybridization technique.

Genomic DNA is isolated from nuclei of subject to be identified. Oligonucleotide probes of approximately 30 bp in length are synthesized that correspond to at least 10, preferably 50 sequences from the 5' ESTs or cDNAs or genomic DNAs obtainable therefrom. The probes are used to hybridize to the genomic DNA through conditions known to those in the art. The oligonucleotides are end labeled with P<sup>32</sup> using polynucleotide kinase (Pharmacia). Dot Blots are created by spotting the genomic DNA onto nitrocellulose or the like using a vacuum dot blot manifold (BioRad, Richmond California). The nitrocellulose filter containing the genomic sequences is baked or UV linked to the filter, prehybridized and hybridized with labeled probe using techniques known in the art (Davis et al., supra). The <sup>32</sup>P

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labeled DNA fragments are sequentially hybridized with successively stringent conditions to detect minimal differences between the 30 bp sequence and the DNA. Tetramethylammonium chloride is useful for identifying clones containing small numbers of nucleotide mismatches (Wood et al., Proc. Natl. Acad. Sci. USA 82(6):1585-1588, 1985) which is hereby incorporated by reference. A unique pattern of dots distinguishes one individual from another individual.

5' EST sequences (or cDNAs or genomic DNAs obtainable therefrom) or oligonucleotides containing at least 10 consecutive bases from these sequences can be used as probes in the following alternative fingerprinting technique. Preferably, the probe comprises at least 12, 15, or 17 consecutive nucleotides from the 5' EST sequences (or cDNAs or genomic DNAs obtainable therefrom). More preferably, the probe comprises at least 20-30 consecutive nucleotides from the 5' EST sequences (or cDNAs or genomic DNAs obtainable therefrom). In some embodiments, the probe comprises more than 30 nucleotides from the 5' EST sequences (or cDNAs or genomic DNAs obtainable therefrom).

Preferably, a plurality of probes having sequences from different genes are used in the alternative fingerprinting technique. Example 50 below provides a representative alternative fingerprinting procedure in which the probes are derived from 5'EST.

#### **EXAMPLE 50**

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#### Alternative "Fingerprint" Identification Technique

20-mer oligonucleotides are prepared from a large number, e.g. 50, 100, or 200, of 5'EST using commercially available oligonucleotide services such as Genset, Paris, France. Cell samples from the test subject are processed for DNA using techniques well known to those with skill in the art. The nucleic acid is digested with restriction enzymes such as EcoRI and XbaI. Following digestion, samples are applied to wells for electrophoresis. The procedure, as known in the art, may be modified to accommodate polyacrylamide electrophoresis, however in this example, samples containing 5 ug of DNA are loaded into wells and separated on 0.8% agarose gels. The gels are transferred onto nitrocellulose using standard Southern blotting techniques.

10 ng of each of the oligonucleotides are pooled and end-labeled with <sup>32</sup>P. The nitrocellulose is prehybridized with blocking solution and hybridized with the labeled probes.

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Following hybridization and washing, the nitrocellulose filter is exposed to X-Omat AR X-ray film. The resulting hybridization pattern will be unique for each individual.

It is additionally contemplated within this example that the number of probe sequences used can be varied for additional accuracy or clarity.

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The proteins encoded by the extended cDNAs may also be used to generate antibodies as explained in Examples 30 and 43 in order to identify the tissue type or cell species from which a sample is derived as described in example 51.

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#### **EXAMPLE 51**

# Identification of Tissue Types or Cell Species by Means of Labeled Tissue Specific Antibodies

Identification of specific tissues is accomplished by the visualization of tissue specific antigens by means of antibody preparations according to Examples 30 and 43 which are conjugated, directly or indirectly to a detectable marker. Selected labeled antibody species bind to their specific antigen binding partner in tissue sections, cell suspensions, or in extracts of soluble proteins from a tissue sample to provide a pattern for qualitative or semi-qualitative interpretation.

Antisera for these procedures must have a potency exceeding that of the native preparation, and for that reason, antibodies are concentrated to a mg/ml level by isolation of the gamma globulin fraction, for example, by ion-exchange chromatography or by ammonium sulfate fractionation. Also, to provide the most specific antisera, unwanted antibodies, for example to common proteins, must be removed from the gamma globulin fraction, for example by means of insoluble immunoabsorbents, before the antibodies are labeled with the marker. Either monoclonal or heterologous antisera is suitable for either procedure.

### A. Immunohistochemical techniques

Purified, high-titer antibodies, prepared as described above, are conjugated to a detectable marker, as described, for example, by Fudenberg, Chap. 26 in: *Basic and Clinical Immunology*, 3rd Ed. Lange, Los Altos, California, 1980, or Rose, *et al.*, Chap. 12 in: *Methods in Immunodiagnosis*, 2d Ed. John Wiley and Sons, New York (1980), the disclosures of which are incorporated herein by reference.

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A fluorescent marker, either fluorescein or rhodamine, is preferred, but antibodies can also be labeled with an enzyme that supports a color producing reaction with a substrate, such as horseradish peroxidase. Markers can be added to tissue-bound antibody in a second step, as described below. Alternatively, the specific antitissue antibodies can be labeled with ferritin or other electron dense particles, and localization of the ferritin coupled antigen-antibody complexes achieved by means of an electron microscope. In yet another approach, the antibodies are radiolabeled, with, for example <sup>125</sup>I, and detected by overlaying the antibody treated preparation with photographic emulsion.

Preparations to carry out the procedures can comprise monoclonal or polyclonal antibodies to a single protein or peptide identified as specific to a tissue type, for example, brain tissue, or antibody preparations to several antigenically distinct tissue specific antigens can be used in panels, independently or in mixtures, as required.

Tissue sections and cell suspensions are prepared for immunohistochemical examination according to common histological techniques. Multiple cryostat sections (about 4 µm, unfixed) of the unknown tissue and known control, are mounted and each slide covered with different dilutions of the antibody preparation. Sections of known and unknown tissues should also be treated with preparations to provide a positive control, a negative control, for example, pre-immune sera, and a control for non-specific staining, for example, buffer.

Treated sections are incubated in a humid chamber for 30 min at room temperature, rinsed, then washed in buffer for 30-45 min. Excess fluid is blotted away, and the marker developed.

If the tissue specific antibody was not labeled in the first incubation, it can be labeled at this time in a second antibody-antibody reaction, for example, by adding fluorescein- or enzyme-conjugated antibody against the immunoglobulin class of the antiserum-producing species, for example, fluorescein labeled antibody to mouse IgG. Such labeled sera are commercially available.

The antigen found in the tissues by the above procedure can be quantified by measuring the intensity of color or fluorescence on the tissue section, and calibrating that signal using appropriate standards.

### B. Identification of tissue specific soluble proteins

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The visualization of tissue specific proteins and identification of unknown tissues from that procedure is carried out using the labeled antibody reagents and detection strategy as described for immunohistochemistry; however the sample is prepared according to an electrophoretic technique to distribute the proteins extracted from the tissue in an orderly array on the basis of molecular weight for detection.

A tissue sample is homogenized using a Virtis apparatus; cell suspensions are disrupted by Dounce homogenization or osmotic lysis, using detergents in either case as required to disrupt cell membranes, as is the practice in the art. Insoluble cell components such as nuclei, microsomes, and membrane fragments are removed by ultracentrifugation, and the soluble protein-containing fraction concentrated if necessary and reserved for analysis.

A sample of the soluble protein solution is resolved into individual protein species by conventional SDS polyacrylamide electrophoresis as described, for example, by Davis, et al., Section 19-2 in: Basic Methods in Molecular Biology, Leder ed., Elsevier, New York, 1986, the disclosure of which is incorporated herein by reference, using a range of amounts of polyacrylamide in a set of gels to resolve the entire molecular weight range of proteins to be detected in the sample. A size marker is run in parallel for purposes of estimating molecular weights of the constituent proteins. Sample size for analysis is a convenient volume of from 5 to 55  $\mu$ l, and containing from about 1 to 100  $\mu$ g protein. An aliquot of each of the resolved proteins is transferred by blotting to a nitrocellulose filter paper, a process that maintains the pattern of resolution. Multiple copies are prepared. The procedure, known as Western Blot Analysis, is well described in Davis, L. et al., supra Section 19-3. One set of nitrocellulose blots is stained with Coomassie blue dye to visualize the entire set of proteins for comparison with the antibody bound proteins. The remaining nitrocellulose filters are then incubated with a solution of one or more specific antisera to tissue specific proteins prepared as described in Examples 30 and 43. In this procedure, as in procedure A above, appropriate positive and negative sample and reagent controls are run.

In either procedure A or B, a detectable label can be attached to the primary tissue antigen-primary antibody complex according to various strategies and permutations thereof. In a straightforward approach, the primary specific antibody can be labeled, alternatively, the unlabeled complex can be bound by a labeled secondary anti-IgG antibody. In other

approaches, either the primary or secondary antibody is conjugated to a biotin molecule, which can, in a subsequent step, bind an avidin conjugated marker. According to yet another strategy, enzyme labeled or radioactive protein A, which has the property of binding to any IgG, is bound in a final step to either the primary or secondary antibody.

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The visualization of tissue specific antigen binding at levels above those seen in control tissues to one or more tissue specific antibodies, prepared from the gene sequences identified from extended cDNA sequences, can identify tissues of unknown origin, for example, forensic samples, or differentiated tumor tissue that has metastasized to foreign bodily sites.

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In addition to their applications in forensics and identification, 5' ESTs (or cDNAs or genomic DNAs obtainable therefrom) may be mapped to their chromosomal locations. Example 52 below describes radiation hybrid (RH) mapping of human chromosomal regions using 5'ESTs. Example 53 below describes a representative procedure for mapping an 5' EST to its location on a human chromosome. Example 54 below describes mapping of 5' ESTs on metaphase chromosomes by Fluorescence In Situ Hybridization (FISH). Those skilled in the art will appreciate that the method of Examples 52-54 may also be used to map cDNAs or genomic DNAs obtainable from the 5' ESTs to their chromosomal locations.

## 2. Use of 5' ESTs or Sequences Obtainable Therefrom or Portions Thereof in Chromosome Mapping

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#### **EXAMPLE 52**

#### Radiation hybrid mapping of 5'ESTs to the human genome

Radiation hybrid (RH) mapping is a somatic cell genetic approach that can be used for high resolution mapping of the human genome. In this approach, cell lines containing one or more human chromosomes are lethally irradiated, breaking each chromosome into fragments whose size depends on the radiation dose. These fragments are rescued by fusion with cultured rodent cells, yielding subclones containing different portions of the human genome. This technique is described by Benham et al., Genomics 4:509-517, 1989; and Cox et al., Science 250:245-250, 1990, the entire contents of which are hereby incorporated by reference. The random and independent nature of the subclones permits efficient mapping of

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any human genome marker. Human DNA isolated from a panel of 80-100 cell lines provides a mapping reagent for ordering 5'EST. In this approach, the frequency of breakage between markers is used to measure distance, allowing construction of fine resolution maps as has been done using conventional ESTs (Schuler et al., Science 274:540-546, 1996, hereby incorporated by reference).

RH mapping has been used to generate a high-resolution whole genome radiation hybrid map of human chromosome 17q22-q25.3 across the genes for growth hormone (GH) and thymidine kinase (TK) (Foster et al., Genomics 33:185-192, 1996), the region surrounding the Gorlin syndrome gene (Obermayr et al., Eur. J. Hum. Genet. 4:242-245, 1996), 60 loci covering the entire short arm of chromosome 12 (Raeymaekers et al., Genomics 29:170-178, 1995), the region of human chromosome 22 containing the neurofibromatosis type 2 locus (Frazer et al., Genomics 14:574-584, 1992) and 13 loci on the long arm of chromosome 5 (Warrington et al., Genomics 11:701-708, 1991).

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#### **EXAMPLE 53**

### Mapping of 5'ESTs to HumanChromosomes using PCR techniques

5' ESTs (or cDNAs or genomic DNAs obtainable therefrom) may be assigned to human chromosomes using PCR based methodologies. In such approaches, oligonucleotide primer pairs are designed from the 5' ESTs (or cDNAs or genomic DNAs obtainable therefrom) to minimize the chance of amplifying through an intron. Preferably, the oligonucleotide primers are 18-23 bp in length and are designed for PCR amplification. The creation of PCR primers from known sequences is well known to those with skill in the art. For a review of PCR technology see Erlich in PCR Technology, Principles and Applications for DNA Amplification, Freeman and Co., New York, 1992, the disclosure of which is incorporated herein by reference.

The primers are used in polymerase chain reactions (PCR) to amplify templates from total human genomic DNA. PCR conditions are as follows: 60 ng of genomic DNA is used as a template for PCR with 80 ng of each oligonucleotide primer, 0.6 unit of Taq polymerase, and 1 μCu of a <sup>32</sup>P-labeled deoxycytidine triphosphate. The PCR is performed in a microplate thermocycler (Techne) under the following conditions: 30 cycles of 94°C, 1.4 min; 55°C, 2 min; and 72°C, 2 min; with a final extension at 72°C for 10 min. The amplified

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products are analyzed on a 6% polyacrylamide sequencing gel and visualized by autoradiography. If the length of the resulting PCR product is identical to the distance between the ends of the primer sequences in the extended cDNA from which the primers are derived, then the PCR reaction is repeated with DNA templates from two panels of human-rodent somatic cell hybrids, BIOS PCRable DNA (BIOS Corporation) and NIGMS Human-Rodent Somatic Cell Hybrid Mapping Panel Number 1 (NIGMS, Camden, NJ).

PCR is used to screen a series of somatic cell hybrid cell lines containing defined sets of human chromosomes for the presence of a given 5' EST (or cDNA or genomic DNA obtainable therefrom). DNA is isolated from the somatic hybrids and used as starting templates for PCR\_reactions using the primer pairs from the 5' EST (or cDNA or genomic DNA obtainable therefrom). Only those somatic cell hybrids with chromosomes containing the human gene corresponding to the 5' EST (or cDNA or genomic DNA obtainable therefrom) will yield an amplified fragment. The 5' EST (or cDNA or genomic DNA obtainable therefrom) are assigned to a chromosome by analysis of the segregation pattern of PCR products from the somatic hybrid DNA templates. The single human chromosome present in all cell hybrids that give rise to an amplified fragment is the chromosome containing that 5'EST (or cDNA or genomic DNA obtainable therefrom). For a review of techniques and analysis of results from somatic cell gene mapping experiments, see Ledbetter et al., Genomics 6:475-481, 1990, the disclosure of which is incorporated herein by reference.

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#### **EXAMPLE 54**

## Mapping of Extended 5' ESTs to Chromosomes Using Fluorescence In Situs Hybridization

Fluorescence in situ hybridization allows the 5'EST (or cDNA or genomic DNA obtainable therefrom) to be mapped to a particular location on a given chromosome. The chromosomes to be used for fluorescence in situ hybridization techniques may be obtained from a variety of sources including cell cultures, tissues, or whole blood.

In a preferred embodiment, chromosomal localization of an 5'EST (or cDNA or genomic DNA obtainable therefrom) is obtained by FISH as described by Cherif *et al.* (*Proc. Natl. Acad. Sci. U.S.A.*, 87:6639-6643, 1990), the disclosure of which is incorporated herein by reference. Metaphase chromosomes are prepared from phytohemagglutinin (PHA)-

stimulated blood cell donors. PHA-stimulated lymphocytes from healthy males are cultured for 72 h in RPMI-1640 medium. For synchronization, methotrexate (10 µM) is added for 17 h, followed by addition of 5-bromodeoxyuridine (5-BrdU, 0.1 mM) for 6 h. Colcemid (1 µg/ml) is added for the last 15 min before harvesting the cells. Cells are collected, washed in RPMI, incubated with a hypotonic solution of KCl (75 mM) at 37°C for 15 min and fixed in three changes of methanol:acetic acid (3:1). The cell suspension is dropped onto a glass slide and air dried. The 5'EST (or cDNA or genomic DNA obtainable therefrom) is labeled with biotin-16 dUTP by nick translation according to the manufacturer's instructions (Bethesda Research Laboratories, Bethesda, MD), purified using a Sephadex G-50 column (Pharmacia, Upsala, Sweden) and precipitated. Just prior to hybridization, the DNA pellet is dissolved in hybridization buffer (50% formamide, 2 X SSC, 10% dextran sulfate, 1 mg/ml sonicated salmon sperm DNA, pH 7) and the probe is denatured at 70°C for 5-10 min.

Slides kept at -20°C are treated for 1 h at 37°C with RNase A (100 µg/ml), rinsed three times in 2 X SSC and dehydrated in an ethanol series. Chromosome preparations are denatured in 70% formamide, 2 X SSC for 2 min at 70°C, then dehydrated at 4°C. The slides are treated with proteinase K (10 µg/100 ml in 20 mM Tris-HCl, 2 mM CaCl<sub>2</sub>) at 37°C for 8 min and dehydrated. The hybridization mixture containing the probe is placed on the slide, covered with a coverslip, sealed with rubber cement and incubated overnight in a humid chamber at 37°C. After hybridization and post-hybridization washes, the biotinylated probe is detected by avidin-FITC and amplified with additional layers of biotinylated goat anti-avidin and avidin-FITC. For chromosomal localization, fluorescent R-bands are obtained as previously described (Cherif et al., supra.). The slides are observed under a LEICA fluorescence microscope (DMRXA). Chromosomes are counterstained with propidium iodide and the fluorescent signal of the probe appears as two symmetrical yellow-green spots on both chromatids of the fluorescent R-band chromosome (red). Thus, a particular 5'EST (or cDNA or genomic DNA obtainable therefrom) may be localized to a particular cytogenetic R-band on a given chromosome.

Once the 5'EST (or cDNA or genomic DNA obtainable therefrom) have been assigned to particular chromosomes using the techniques described in Examples 52-54 above,

they may be utilized to construct a high resolution map of the chromosomes on which they are located or to identify the chromosomes in a sample.

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#### Use of 5'EST to Construct or Expand Chromosome Maps

Chromosome mapping involves assigning a given unique sequence to a particular chromosome as described above. Once the unique sequence has been mapped to a given chromosome, it is ordered relative to other unique sequences located on the same chromosome. One approach to chromosome mapping utilizes a series of yeast artificial chromosomes (YACs) bearing several thousand long inserts derived from the chromosomes of the organism from which the extended cDNAs (or genomic DNAs obtainable therefrom) are obtained. This approach is described in Nagaraja et al., Genome Research 7:210-222, 1997, the disclosure of which is incorporated herein by reference. Briefly, in this approach each chromosome is broken into overlapping pieces which are inserted into the YAC vector. The YAC inserts are screened using PCR or other methods to determine whether they include the 5'EST (or cDNA or genomic DNA obtainable therefrom) whose position is to be determined. Once an insert has been found which includes the 5'EST (or cDNA or genomic DNA obtainable therefrom), the insert can be analyzed by PCR or other methods to determine whether the insert also contains other sequences known to be on the chromosome or in the region from which the 5'EST (or cDNA or genomic DNA obtainable therefrom) was derived. This process can be repeated for each insert in the YAC library to determine the location of each of the extended cDNAs (or genomic DNAs obtainable therefrom) relative to one another and to other known chromosomal markers. In this way, a high resolution map of the distribution of numerous unique markers along each of the organisms chromosomes may be obtained.

As described in Example 56 below extended cDNAs (or genomic DNAs obtainable therefrom) may also be used to identify genes associated with a particular phenotype, such as hereditary disease or drug response.

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# 3. Use of 5'ESTs or Sequences Obtained Therefrom or Fragments Thereof in Gene Identification

#### **EXAMPLE 56**

Identification of genes associated with hereditary diseases or drug response

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This example illustrates an approach useful for the association of 5'ESTs (or cDNA or genomic DNA obtainable therefrom) with particular phenotypic characteristics. In this example, a particular 5'EST (or cDNA or genomic DNA obtainable therefrom) is used as a test probe to associate that 5'EST (or cDNA or genomic DNA obtainable therefrom) with a particular phenotypic characteristic.

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5'ESTs (or cDNA or genomic DNA obtainable therefrom) are mapped to a particular location on a human chromosome using techniques such as those described in Examples 52 and 53 or other techniques known in the art. A search of Mendelian Inheritance in Man (McKusick in *Mendelian Inheritance in Man* (available on line through Johns Hopkins University Welch Medical Library) reveals the region of the human chromosome which contains the 5'EST (or cDNA or genomic DNA obtainable therefrom) to be a very gene rich region containing several known genes and several diseases or phenotypes for which genes have not been identified. The gene corresponding to this 5'EST (or cDNA or genomic DNA obtainable therefrom) thus becomes an immediate candidate for each of these genetic diseases

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Cells from patients with these diseases or phenotypes are isolated and expanded in culture. PCR primers from the 5'EST (or cDNA or genomic DNA obtainable therefrom) are used to screen genomic DNA, mRNA or cDNA obtained from the patients. 5'ESTs (or cDNA or genomic DNA obtainable therefrom) that are not amplified in the patients can be positively associated with a particular disease by further analysis. Alternatively, the PCR analysis may yield fragments of different lengths when the samples are derived from an individual having the phenotype associated with the disease than when the sample is derived from a healthy individual, indicating that the gene containing the 5'EST may be responsible for the genetic disease.

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### VI. Use f5'EST (or cDNA or Genomic DNA Obtainable Therefrom) to Construct Vectors

The present 5'ESTs (or cDNA or genomic DNA obtainable therefrom) may also be used to construct secretion vectors capable of directing the secretion of the proteins encoded by genes therein. Such secretion vectors may facilitate the purification or enrichment of the proteins encoded by genes inserted therein by reducing the number of background proteins from which the desired protein must be purified or enriched. Exemplary secretion vectors are described in Example 57 below.

#### 10 <u>1. Construction of Secretion Vectors</u>

#### **EXAMPLE 57**

#### Construction of Secretion Vectors

The secretion vectors include a promoter capable of directing gene expression in the host cell, tissue, or organism of interest. Such promoters include the Rous Sarcoma Virus promoter, the SV40 promoter, the human cytomegalovirus promoter, and other promoters familiar to those skilled in the art.

A signal sequence from a 5' EST (or cDNAs or genomic DNAs obtainable therefrom) is operably linked to the promoter such that the mRNA transcribed from the promoter will direct the translation of the signal peptide. The host cell, tissue, or organism may be any cell, tissue, or organism which recognizes the signal peptide encoded by the signal sequence in the 5' EST (or cDNA or genomic DNA obtainable therefrom). Suitable hosts include mammalian cells, tissues or organisms, avian cells, tissues, or organisms, insect cells, tissues or organisms, or yeast.

In addition, the secretion vector contains cloning sites for inserting genes encoding the proteins which are to be secreted. The cloning sites facilitate the cloning of the insert gene in frame with the signal sequence such that a fusion protein in which the signal peptide is fused to the protein encoded by the inserted gene is expressed from the mRNA transcribed from the promoter. The signal peptide directs the extracellular secretion of the fusion protein.

The secretion vector may be DNA or RNA and may integrate into the chromosome of the host, be stably maintained as an extrachromosomal replicon in the host, be an artificial chromosome, or be transiently present in the host. Many nucleic acid backbones suitable for

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use as secretion vectors are known to those skilled in the art, including retroviral vectors, SV40 vectors, Bovine Papilloma Virus vectors, yeast integrating plasmids, yeast episomal plasmids, yeast artificial chromosomes, human artificial chromosomes, P element vectors, baculovirus vectors, or bacterial plasmids capable of being transiently introduced into the host.

The secretion vector may also contain a polyA signal such that the polyA signal is located downstream of the gene inserted into the secretion vector.

After the gene encoding the protein for which secretion is desired is inserted into the secretion vector, the secretion vector is introduced into the host cell, tissue, or organism using calcium phosphate precipitation, DEAE-Dextran, electroporation, liposome-mediated transfection, viral particles or as naked DNA. The protein encoded by the inserted gene is then purified or enriched from the supernatant using conventional techniques such as ammonium sulfate precipitation, immunoprecipitation, immunochromatography, size exclusion chromatography, ion exchange chromatography, and HPLC. Alternatively, the secreted protein may be in a sufficiently enriched or pure state in the supernatant or growth media of the host to permit it to be used for its intended purpose without further enrichment.

The signal sequences may also be inserted into vectors designed for gene therapy. In such vectors, the signal sequence is operably linked to a promoter such that mRNA transcribed from the promoter encodes the signal peptide. A cloning site is located downstream of the signal sequence such that a gene encoding a protein whose secretion is desired may readily be inserted into the vector and fused to the signal sequence. The vector is introduced into an appropriate host cell. The protein expressed from the promoter is secreted extracellularly, thereby producing a therapeutic effect.

The 5' ESTs may also be used to clone sequences located upstream of the 5' ESTs which are capable of regulating gene expression, including promoter sequences, enhancer sequences, and other upstream sequences which influence transcription or translation levels. Once identified and cloned, these upstream regulatory sequences may be used in expression vectors designed to direct the expression of an inserted gene in a desired spatial, temporal, developmental, or quantitative fashion. Example 58 describes a method for cloning sequences upstream of the extended cDNAs or 5' ESTs.

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#### 2. Identification of Upstream Sequences With Promoting or Regulatory Activities

#### **EXAMPLE 58**

Use of Extended cDNAs or 5' ESTs to Clone Upstream Sequences from Genomic DNA

Sequences derived from extended cDNAs or 5' ESTs may be used to isolate the promoters of the corresponding genes using chromosome walking techniques. In one chromosome walking technique, which utilizes the GenomeWalker<sup>TM</sup> kit available from Clontech, five complete genomic DNA samples are each digested with a different restriction enzyme which has a 6 base recognition site and leaves a blunt end. Following digestion, oligonucleotide adapters are ligated to each end of the resulting genomic DNA fragments.

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For each of the five genomic DNA libraries, a first PCR reaction is performed according to the manufacturer's instructions (which are incorporated herein by reference) using an outer adaptor primer provided in the kit and an outer gene specific primer. The gene specific primer should be selected to be specific for the extended cDNA or 5' EST of interest and should have a melting temperature, length, and location in the extended cDNA or 5'EST which is consistent with its use in PCR reactions. Each first PCR reaction contains 5 ng of genomic DNA, 5 µl of 10X Tth reaction buffer, 0.2 mM of each dNTP, 0.2 µM each of outer adaptor primer and outer gene specific primer, 1.1 mM of Mg(OAc)<sub>2</sub>, and 1 µl of the Tth polymerase 50X mix in a total volume of 50 µl. The reaction cycle for the first PCR reaction is as follows: 1 min - 94°C / 2 sec - 94°C, 3 min - 72°C (7 cycles) / 2 sec - 94°C, 3 min - 67°C.

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The product of the first PCR reaction is diluted and used as a template for a second PCR reaction according to the manufacturer's instructions using a pair of nested primers which are located internally on the amplicon resulting from the first PCR reaction. For example, 5 µl of the reaction product of the first PCR reaction mixture may be diluted 180 times. Reactions are made in a 50 µl volume having a composition identical to that of the first PCR reaction except the nested primers are used. The first nested primer is specific for the adaptor, and is provided with the GenomeWalker<sup>TM</sup> kit. The second nested primer is specific for the particular extended cDNA or 5' EST for which the promoter is to be cloned and should have a melting temperature, length, and location in the extended cDNA or 5' EST which is consistent with its use in PCR

reactions. The reaction parameters of the second PCR reaction are as follows: 1 min - 94°C / 2 sec - 94°C, 3 min - 72°C (6 cycles) / 2 sec - 94°C, 3 min - 67°C (25 cycles) / 5 min - 67°C. The product of the second PCR reaction is purified, cloned, and sequenced using standard techniques.

Alternatively, two or more human genomic DNA libraries can be constructed by using two or more restriction enzymes. The digested genomic DNA is cloned into vectors which can be converted into single stranded, circular, or linear DNA. A biotinylated oligonucleotide comprising at least 15 nucleotides from the extended cDNA or 5' EST sequence is hybridized to the single stranded DNA. Hybrids between the biotinylated oligonucleotide and the single stranded DNA containing the extended cDNA or EST sequence are isolated as described in Example 29 above. Thereafter, the single stranded DNA containing the extended cDNA or EST sequence is released from the beads and converted into double stranded DNA using a primer specific for the extended cDNA or 5' EST sequence or a primer corresponding to a sequence included in the cloning vector. The resulting double stranded DNA is transformed into bacteria. DNAs containing the 5' EST or extended cDNA sequences are identified by colony PCR or colony hybridization.

Once the upstream genomic sequences have been cloned and sequenced as described above, prospective promoters and transcription start sites within the upstream sequences may be identified by comparing the sequences upstream of the extended cDNAs or 5' ESTs with databases containing known transcription start sites, transcription factor binding sites, or promoter sequences.

In addition, promoters in the upstream sequences may be identified using promoter reporter vectors as described in Example .

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#### **EXAMPLE 59**

### Identification of Promoters in Cloned Upstream Sequences

The genomic sequences upstream of the extended cDNAs or 5' ESTs are cloned into a suitable promoter reporter vector, such as the pSEAP-Basic, pSEAP-Enhancer, p $\beta$ gal-Basic, p $\beta$ gal-Enhancer, or pEGFP-1 Promoter Reporter vectors available from Clontech. Briefly, each of these promoter reporter vectors include multiple cloning sites positioned

upstream of a reporter gene encoding a readily assayable protein such as secreted alkaline phosphatase, β galactosidase, or green fluorescent protein. The sequences upstream of the extended cDNAs or 5′ ESTs are inserted into the cloning sites upstream of the reporter gene in both orientations and introduced into an appropriate host cell. The level of reporter protein is assayed and compared to the level obtained from a vector which lacks an insert in the cloning site. The presence of an elevated expression level in the vector containing the insert with respect to the control vector indicates the presence of a promoter in the insert. If necessary, the upstream sequences can be cloned into vectors which contain an enhancer for augmenting transcription levels from weak promoter sequences. A significant level of expression above that observed with the vector lacking an insert indicates that a promoter sequence is present in the inserted upstream sequence.

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Appropriate host cells for the promoter reporter vectors may be chosen based on the results of the above described determination of expression patterns of the extended cDNAs and ESTs. For example, if the expression pattern analysis indicates that the mRNA corresponding to a particular extended cDNA or 5' EST is expressed in fibroblasts, the promoter reporter vector may be introduced into a human fibroblast cell line.

Promoter sequences within the upstream genomic DNA may be further defined by constructing nested deletions in the upstream DNA using conventional techniques such as Exonuclease III digestion. The resulting deletion fragments can be inserted into the promoter reporter vector to determine whether the deletion has reduced or obliterated promoter activity. In this way, the boundaries of the promoters may be defined. If desired, potential individual regulatory sites within the promoter may be identified using site directed mutagenesis or linker scanning to obliterate potential transcription factor binding sites within the promoter individually or in combination. The effects of these mutations on transcription levels may be determined by inserting the mutations into the cloning sites in the promoter reporter vectors.

#### **EXAMPLE 60**

#### Cloning and Identification of Promoters

Using the method described in Example 58 above with 5' ESTs, sequences upstream of several genes were obtained. Using the primer pairs GGG AAG ATG GAG ATA GTA

TTG CCT G (SEQ ID NO:29) and CTG CCA TGT ACA TGA TAG AGA GAT TC (SEQ ID NO:30), the promoter having the internal designation P13H2 (SEQ ID NO:31) was obtained.

Using the primer pairs GTA CCA GGGG ACT GTG ACC ATT GC (SEQ ID NO:32) and CTG TGA CCA TTG CTC CCA AGA GAG (SEQ ID NO:33), the promoter having the internal designation P15B4 (SEQ ID NO:34) was obtained.

Using the primer pairs CTG GGA TGG AAG GCA CGG TA (SEQ ID NO:35) and GAG ACC ACA CAG CTA GAC AA (SEQ ID NO:36), the promoter having the internal designation P29B6 (SEQ ID NO:37) was obtained.

Figure 4 provides a schematic description of the promoters isolated and the way they are assembled with the corresponding 5' tags. The upstream sequences were screened for the presence of motifs resembling transcription factor binding sites or known transcription start sites using the computer program MatInspector release 2.0, August 1996.

Table VII describes the transcription factor binding sites present in each of these promoters. The columns labeled matrice provides the name of the MatInspector matrix used. The column labeled position provides the 5' position of the promoter site. Numeration of the sequence starts from the transcription site as determined by matching the genomic sequence with the 5' EST sequence. The column labeled "orientation" indicates the DNA strand on which the site is found, with the + strand being the coding strand as determined by matching the genomic sequence with the sequence of the 5' EST. The column labeled "score" provides the MatInspector score found for this site. The column labeled "length" provides the length of the site in nucleotides. The column labeled "sequence" provides the sequence of the site found.

Bacterial clones containing plasmids containing the promoter sequences described above described above are presently stored in the inventor's laboratories under the internal identification numbers provided above. The inserts may be recovered from the deposited materials by growing an aliquot of the appropriate bacterial clone in the appropriate medium. The plasmid DNA can then be isolated using plasmid isolation procedures familiar to those skilled in the art such as alkaline lysis minipreps or large scale alkaline lysis plasmid isolation procedures. If desired the plasmid DNA may be further enriched by centrifugation on a cesium chloride gradient, size exclusion chromatography, or anion exchange chromatography.

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The plasmid DNA obtained using these procedures may then be manipulated using standard cloning techniques familiar to those skilled in the art. Alternatively, a PCR can be done with primers designed at both ends of the EST insertion. The PCR product which corresponds to the 5' EST can then be manipulated using standard cloning techniques familiar to those skilled in the art.

The promoters and other regulatory sequences located upstream of the extended cDNAs or 5' ESTs may be used to design expression vectors capable of directing the expression of an inserted gene in a desired spatial, temporal, developmental, or quantitative manner. A promoter capable of directing the desired spatial, temporal, developmental, and quantitative patterns may be selected using the results of the expression analysis described in Example 26 above. For example, if a promoter which confers a high level of expression in muscle is desired, the promoter sequence upstream of an extended cDNA or 5' EST derived from an mRNA which is expressed at a high level in muscle, as determined by the method of Example 26, may be used in the expression vector.

Preferably, the desired promoter is placed near multiple restriction sites to facilitate the cloning of the desired insert downstream of the promoter, such that the promoter is able to drive expression of the inserted gene. The promoter may be inserted in conventional nucleic acid backbones designed for extrachromosomal replication, integration into the host chromosomes or transient expression. Suitable backbones for the present expression vectors include retroviral backbones, backbones from eukaryotic episomes such as SV40 or Bovine Papilloma Virus, backbones from bacterial episomes, or artificial chromosomes.

Preferably, the expression vectors also include a polyA signal downstream of the multiple restriction sites for directing the polyadenylation of mRNA transcribed from the gene inserted into the expression vector.

Following the identification of promoter sequences using the procedures of Examples 58-60, proteins which interact with the promoter may be identified as described in Example 61 below.

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#### **EXAMPLE 61**

# Identification of Proteins Which Interact with Promoter Sequences, Upstream Regulatory Sequences, or mRNA

Sequences within the promoter region which are likely to bind transcription factors may be identified by homology to known transcription factor binding sites or through conventional mutagenesis or deletion analyses of reporter plasmids containing the promoter sequence. For example, deletions may be made in a reporter plasmid containing the promoter sequence of interest operably linked to an assayable reporter gene. The reporter plasmids carrying various deletions within the promoter region are transfected into an appropriate host cell and the effects of the deletions on expression levels is assessed. Transcription factor binding sites within the regions in which deletions reduce expression levels may be further localized using site directed mutagenesis, linker scanning analysis, or other techniques familiar to those skilled in the art.

Nucleic acids encoding proteins which interact with sequences in the promoter may be identified using one-hybrid systems such as those described in the manual accompanying the Matchmaker One-Hybrid System kit available from Clontech (Catalog No. K1603-1), the disclosure of which is incorporated herein by reference. Briefly, the Matchmaker One-hybrid system is used as follows. The target sequence for which it is desired to identify binding proteins is cloned upstream of a selectable reporter gene and integrated into the yeast genome. Preferably, multiple copies of the target sequences are inserted into the reporter plasmid in tandem. A library comprised of fusions between cDNAs to be evaluated for the ability to bind to the promoter and the activation domain of a yeast transcription factor, such as GAL4, is transformed into the yeast strain containing the integrated reporter sequence. The yeast are plated on selective media to select cells expressing the selectable marker linked to the promoter sequence. The colonies which grow on the selective media contain genes encoding proteins which bind the target sequence. The inserts in the genes encoding the fusion proteins are further characterized by sequencing. In addition, the inserts may be inserted into expression vectors or *in vitro* transcription vectors. Binding of the polypeptides encoded by the inserts to the promoter DNA may be confirmed by techniques familiar to those skilled in the art, such as gel shift analysis or DNAse protection analysis.

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## VII. Use of 5' ESTs (rcDNAs or Genomic DNAs Obtainable Therefrom) in Gene Therapy

The present invention also comprises the use of 5'ESTs (or cDNA or genomic DNA obtainable therefrom) in gene therapy strategies, including antisense and triple helix strategies as described in Examples 62 and 63 below. In antisense approaches, nucleic acid sequences complementary to an mRNA are hybridized to the mRNA intracellularly, thereby blocking the expression of the protein encoded by the mRNA. The antisense sequences may prevent gene expression through a variety of mechanisms. For example, the antisense sequences may inhibit the ability of ribosomes to translate the mRNA. Alternatively, the antisense sequences may block transport of the mRNA from the nucleus to the cytoplasm, thereby limiting the amount of mRNA available for translation. Another mechanism through which antisense sequences may inhibit gene expression is by interfering with mRNA splicing. In yet another strategy, the antisense nucleic acid may be incorporated in a ribozyme capable of specifically cleaving the target mRNA.

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### **EXAMPLE 62**

### Preparation and Use of Antisense Oligonucleotides

The antisense nucleic acid molecules to be used in gene therapy may be either DNA or RNA sequences. They may comprise a sequence complementary to the sequence of the 5'EST (or cDNA or genomic DNA obtainable therefrom). The antisense nucleic acids should have a length and melting temperature sufficient to permit formation of an intracellular duplex with sufficient stability to inhibit the expression of the mRNA in the duplex. Strategies for designing antisense nucleic acids suitable for use in gene therapy are disclosed in Green et al., Ann. Rev. Biochem. 55:569-597, 1986; and Izant and Weintraub, Cell 36:1007-1015, 1984, which are hereby incorporated by reference.

In some strategies, antisense molecules are obtained from a nucleotide sequence encoding a protein by reversing the orientation of the coding region with respect to a promoter so as to transcribe the opposite strand from that which is normally transcribed in the cell. The antisense molecules may be transcribed using *in vitro* transcription systems such as those which employ T7 or SP6 polymerase to generate the transcript. Another approach

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involves transcription of the antisense nucleic acids *in vivo* by operably linking DNA containing the antisense sequence to a promoter in an expression vector.

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Alternatively, oligonucleotides which are complementary to the strand normally transcribed in the cell may be synthesized *in vitro*. Thus, the antisense nucleic acids are complementary to the corresponding mRNA and are capable of hybridizing to the mRNA to create a duplex. In some embodiments, the antisense sequences may contain modified sugar phosphate backbones to increase stability and make them less sensitive to RNase activity. Examples of modifications suitable for use in antisense strategies are described by Rossi *et al.*, *Pharmacol. Ther.* **50(2)**:245-254, 1991, which is hereby incorporated by reference.

Various types of antisense oligonucleotides complementary to the sequence of the 5'EST (or cDNA or genomic DNA obtainable therefrom) may be used. In one preferred embodiment, stable and semi-stable antisense oligonucleotides described in International Application No. PCT WO94/23026, hereby incorporated by reference, are used. In these molecules, the 3' end or both the 3' and 5' ends are engaged in intramolecular hydrogen bonding between complementary base pairs. These molecules are better able to withstand exonuclease attacks and exhibit increased stability compared to conventional antisense oligonucleotides.

In another preferred embodiment, the antisense oligodeoxynucleotides against herpes simplex virus types 1 and 2 described in International Application No. WO 95/04141, hereby incorporated by reference, are used.

In yet another preferred embodiment, the covalently cross-linked antisense oligonucleotides described in International Application No. WO 96/31523, hereby incorporated by reference, are used. These double- or single-stranded oligonucleotides comprise one or more, respectively, inter- or intra-oligonucleotide covalent cross-linkages, wherein the linkage consists of an amide bond between a primary amine group of one strand and a carboxyl group of the other strand or of the same strand, respectively, the primary amine group being directly substituted in the 2' position of the strand nucleotide monosaccharide ring, and the carboxyl group being carried by an aliphatic spacer group substituted on a nucleotide or nucleotide analog of the other strand or the same strand, respectively.

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The antisense oligodeoxynucleotides and oligonucleotides disclosed in International Application No. WO 92/18522, incorporated by reference, may also be used. These molecules are stable to degradation and contain at least one transcription control recognition sequence which binds to control proteins and are effective as decoys therefore. These molecules may contain "hairpin" structures, "dumbbell" structures, "modified dumbbell" structures, "cross-linked" decoy structures and "loop" structures.

In another preferred embodiment, the cyclic double-stranded oligonucleotides described in European Patent Application No. 0 572 287 A2, hereby incorporated by reference are used. These ligated oligonucleotide "dumbbells" contain the binding site for a transcription factor and inhibit expression of the gene under control of the transcription factor by sequestering the factor.

Use of the closed antisense oligonucleotides disclosed in International Application No. WO 92/19732, hereby incorporated by reference, is also contemplated. Because these molecules have no free ends, they are more resistant to degradation by exonucleases than are conventional oligonucleotides. These oligonucleotides may be multifunctional, interacting with several regions which are not adjacent to the target mRNA.

The appropriate level of antisense nucleic acids required to inhibit gene expression may be determined using *in vitro* expression analysis. The antisense molecule may be introduced into the cells by diffusion, injection, infection, transfection or h-region-mediated import using procedures known in the art. For example, the antisense nucleic acids can be introduced into the body as a bare or naked oligonucleotide, oligonucleotide encapsulated in lipid, oligonucleotide sequence encapsidated by viral protein, or as an oligonucleotide operably linked to a promoter contained in an expression vector. The expression vector may be any of a variety of expression vectors known in the art, including retroviral or viral vectors, vectors capable of extrachromosomal replication, or integrating vectors. The vectors may be DNA or RNA.

The antisense molecules are introduced onto cell samples at a number of different concentrations preferably between  $1\times10^{-10}$ M to  $1\times10^{-4}$ M. Once the minimum concentration that can adequately control gene expression is identified, the optimized dose is translated into a dosage suitable for use *in vivo*. For example, an inhibiting concentration in culture of  $1\times10^{-7}$  translates into a dose of approximately 0.6 mg/kg bodyweight. Levels of oligonucleotide

WO 99/06552

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PCT/IB98/01236

approaching 100 mg/kg bodyweight or higher may be possible after testing the toxicity of the oligonucleotide in laboratory animals. It is additionally contemplated that cells from the vertebrate are removed, treated with the antisense oligonucleotide, and reintroduced into the vertebrate.

It is further contemplated that the antisense oligonucleotide sequence is incorporated into a ribozyme sequence to enable the antisense to specifically bind and cleave its target mRNA. For technical applications of ribozyme and antisense oligonucleotides see Rossi et al., supra.

In a preferred application of this invention, the polypeptide encoded by the gene is first identified, so that the effectiveness of antisense inhibition on translation can be monitored using techniques that include but are not limited to antibody-mediated tests such as RIAs and ELISA, functional assays, or radiolabeling.

The 5' ESTs of the present invention (or cDNAs or genomic DNAs obtainable therefrom) may also be used in gene therapy approaches based on intracellular triple helix formation. Triple helix oligonucleotides are used to inhibit transcription from a genome. They are particularly useful for studying alterations in cell activity as it is associated with a particular gene. The 5' EST sequences (or cDNAs or genomic DNAs obtainable therefrom) of the present invention or, more preferably, a portion of those sequences, can be used to inhibit gene expression in individuals having diseases associated with expression of a particular gene. Similarly, a portion of 5' EST sequences (or cDNAs or genomic DNAs obtainable therefrom) can be used to study the effect of inhibiting transcription of a particular gene within a cell. Traditionally, homopurine sequences were considered the most useful for triple helix strategies. However, homopyrimidine sequences can also inhibit gene expression. Such homopyrimidine oligonucleotides bind the major groove homopurine:homopyrimidine sequences. Thus, both types of sequences from the 5'EST or from the gene corresponding to the 5'EST are contemplated within the scope of this invention.

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#### **EXAMPLE 63**

### Preparation and Use of Triple Helix Probes

The sequences of the 5' ESTs (or cDNAs or genomic DNAs obtainable therefrom) are scanned to identify 10-mer to 20-mer homopyrimidine or homopurine stretches which could be used in triple-helix based strategies for inhibiting gene expression. Following identification of candidate homopyrimidine or homopurine stretches, their efficiency in inhibiting gene expression is assessed by introducing varying amounts of oligonucleotides containing the candidate sequences into tissue culture cells which normally express the target gene. The oligonucleotides may be prepared on an oligonucleotide synthesizer or they may be purchased commercially from a company specializing in custom oligonucleotide synthesis, such as GENSET, Paris, France.

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The oligonucleotides may be introduced into the cells using a variety of methods known to those skilled in the art, including but not limited to calcium phosphate precipitation, DEAE-Dextran, electroporation, liposome-mediated transfection or native uptake.

Treated cells are monitored for altered cell function or reduced gene expression using techniques such as Northern blotting, RNase protection assays, or PCR based strategies to monitor the transcription levels of the target gene in cells which have been treated with the oligonucleotide. The cell functions to be monitored are predicted based upon the homologies of the target gene corresponding to the extended cDNA from which the oligonucleotide was derived with known gene sequences that have been associated with a particular function. The cell functions can also be predicted based on the presence of abnormal physiologies within cells derived from individuals with a particular inherited disease, particularly when the extended cDNA is associated with the disease using techniques described in Example 56.

The oligonucleotides which are effective in inhibiting gene expression in tissue culture cells may then be introduced *in vivo* using the techniques described above and in Example 62 at a dosage calculated based on the *in vitro* results, as described in Example 62.

In some embodiments, the natural (beta) anomers of the oligonucleotide units can be replaced with alpha anomers to render the oligonucleotide more resistant to nucleases. Further, an intercalating agent such as ethidium bromide, or the like, can be attached to the 3' end of the alpha oligonucleotide to stabilize the triple helix. For information on the

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generation of oligonucleotides suitable for triple helix formation see Griffin *et al.*, *Science* 245:967-971, 1989, which is hereby incorporated by this reference.

#### **EXAMPLE 64**

# Use of cDNAs Obtained Using the 5' ESTs to Express an Encoded Protein in a Host Organism

The cDNAs obtained as described above using the 5' ESTs of the present invention may also be used to express an encoded protein in a host organism to produce a beneficial effect. In such procedures, the encoded protein may be transiently expressed in the host organism or stably expressed in the host organism. The encoded protein may have any of the activities described above. The encoded protein may be a protein which the host organism lacks or, alternatively, the encoded protein may augment the existing levels of the protein in the host organism.

A full length extended cDNA encoding the signal peptide and the mature protein, or an extended cDNA encoding only the mature protein is introduced into the host organism. The extended cDNA may be introduced into the host organism using a variety of techniques known to those of skill in the art. For example, the extended cDNA may be injected into the host organism as naked DNA such that the encoded protein is expressed in the host organism, thereby producing a beneficial effect.

Alternatively, the extended cDNA may be cloned into an expression vector downstream of a promoter which is active in the host organism. The expression vector may be any of the expression vectors designed for use in gene therapy, including viral or retroviral vectors. The expression vector may be directly introduced into the host organism such that the encoded protein is expressed in the host organism to produce a beneficial effect. In another approach, the expression vector may be introduced into cells *in vitro*. Cells containing the expression vector are thereafter selected and introduced into the host organism, where they express the encoded protein to produce a beneficial effect.

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#### **EXAMPLE 65**

# Use of Signal Peptides Encoded by 5' ESTs or Sequences obtained Therefrom to Import Proteins Into Cells

The short core hydrophobic region (h) of signal peptides encoded by the 5'ESTS or extended cDNAs derived from SEQ ID NOs: 38-270 may also be used as a carrier to import a peptide or a protein of interest, so-called cargo, into tissue culture cells (Lin et al., J. Biol. Chem., 270: 14225-14258, 1995; Du et al., J. Peptide Res., 51: 235-243, 1998; Rojas et al., Nature Biotech., 16: 370-375, 1998).

When cell permeable peptides of limited size (approximately up to 25 amino acids) are to be translocated across cell membrane, chemical synthesis may be used in order to add the h region to either the C-terminus or the N-terminus to the cargo peptide of interest. Alternatively, when longer peptides or proteins are to be imported into cells, nucleic acids can be genetically engineered, using techniques familiar to those skilled in the art, in order to link the extended cDNA sequence encoding the h region to the 5' or the 3' end of a DNA sequence coding for a cargo polypeptide. Such genetically engineered nucleic acids are then translated either *in vitro* or *in vivo* after transfection into appropriate cells, using conventional techniques to produce the resulting cell permeable polypeptide. Suitable hosts cells are then simply incubated with the cell permeable polypeptide which is then translocated across the membrane.

This method may be applied to study diverse intracellular functions and cellular processes. For instance, it has been used to probe functionally relevant domains of intracellular proteins and to examine protein-protein interactions involved in signal transduction pathways (Lin et al., supra; Lin et al., J. Biol. Chem., 271: 5305-5308, 1996; Rojas et al., J. Biol. Chem., 271: 27456-27461, 1996; Liu et al., Proc. Natl. Acad. Sci. USA, 93: 11819-11824, 1996; Rojas et al., Bioch. Biophys. Res. Commun., 234: 675-680, 1997).

Such techniques may be used in cellular therapy to import proteins producing therapeutic effects. For instance, cells isolated from a patient may be treated with imported therapeutic proteins and then re-introduced into the host organism.

Alternatively, the h region of signal peptides of the present invention could be used in combination with a nuclear localization signal to deliver nucleic acids into cell nucleus. Such oligonucleotides may be antisense oligonucleotides or oligonucleotides designed to form

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triple helixes, as described in examples 62 and 63 respectively, in order to inhibit processing and/or maturation of a target cellular RNA.

As discussed above, the cDNAs or portions thereof obtained using the 5' ESTs of the present invention can be used for various purposes. The polynucleotides can be used to express recombinant protein for analysis, characterization or therapeutic use; as markers for tissues in which the corresponding protein is preferentially expressed (either constitutively or at a particular stage of tissue differentiation or development or in disease states); as molecular weight markers on Southern gels; as chromosome markers or tags (when labeled) to identify chromosomes or to map related gene positions; to compare with endogenous DNA sequences in patients to identify potential genetic disorders; as probes to hybridize and thus discover novel, related DNA sequences; as a source of information to derive PCR primers for genetic fingerprinting; for selecting and making oligomers for attachment to a "gene chip" or other support, including for examination for expression patterns; to raise anti-protein antibodies using DNA immunization techniques; and as an antigen to raise anti-DNA antibodies or elicit another immune response. Where the polynucleotide encodes a protein which binds or potentially binds to another protein (such as, for example, in a receptor-ligand interaction), the polynucleotide can also be used in interaction trap assays (such as, for example, that described in Gyuris et al., Cell 75:791-803, 1993, the disclosure of which is hereby incorporated by reference) to identify polynucleotides encoding the other protein with which binding occurs or to identify inhibitors of the binding interaction.

The proteins or polypeptides provided by the present invention can similarly be used in assays to determine biological activity, including in a panel of multiple proteins for high-throughput screening; to raise antibodies or to elicit another immune response; as a reagent (including the labeled reagent) in assays designed to quantitatively determine levels of the protein (or its receptor) in biological fluids; as markers for tissues in which the corresponding protein is preferentially expressed (either constitutively or at a particular stage of tissue differentiation or development or in a disease state); and, of course, to isolate correlative receptors or ligands. Where the protein binds or potentially binds to another protein (such as, for example, in a receptor-ligand interaction), the protein can be used to identify the other protein with which binding occurs or to identify inhibitors of the binding interaction. Proteins

involved in these binding interactions can also be used to screen for peptide or small molecule inhibitors or agonists of the binding interaction.

Any or all of these research utilities are capable of being developed into reagent grade or kit format for commercialization as research products.

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Methods for performing the uses listed above are well known to those skilled in the art. References disclosing such methods include without limitation *Molecular Cloning*; A Laboratory Manual, 2d ed., Cold Spring Harbor Laboratory Press, Sambrook, Fritsch and Maniatis eds., 1989, and Methods in Enzymology; Guide to Molecular Cloning Techniques, Academic Press, Berger and Kimmel eds., 1987.

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Polynucleotides and proteins of the present invention can also be used as nutritional sources or supplements. Such uses include without limitation use as a protein or amino acid supplement, use as a carbon source, use as a nitrogen source and use as a source of carbohydrate. In such cases the protein or polynucleotide of the invention can be added to the feed of a particular organism or can be administered as a separate solid or liquid preparation, such as in the form of powder, pills, solutions, suspensions or capsules. In the case of microorganisms, the protein or polynucleotide of the invention can be added to the medium in or on which the microorganism is cultured.

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Although this invention has been described in terms of certain preferred embodiments, other embodiments which will be apparent to those of ordinary skill in the art in view of the disclosure herein are also within the scope of this invention. Accordingly, the scope of the invention is intended to be defined only by reference to the appended claims. All documents cited herein are incorporated herein by reference in their entirety.

	Search characteristic	acteristic	Selection	Selection Characteristics	5
Step	Program	Strand	Parameters	Identity (%)	Length (bp)
miscellanaeous	blastn	both	S=61 X=16	06	17
trnA	fasta	both		80	09
IRNA	blastn	both	S=108	80	40
mtRNA	blastn	both	S=108	80	40
Procaryotic	blastn	both	S=144	06	40
Fungal	blastn	both	S=144	06	40
Alu	fasta*	both	•	70	40
[1	blastn	both	S=72	70	40
Repeats	blastn	both	S=72	70	40
Promoters	blastn	top	S=54 X=16	06	15†
Vertebrate	fasta*	both	S=108	90	30
ESTs	blastn	both	S=108 X=16	06	30
Proteins	blastx¤	top	E = 0.001	1	-

Table 1: Parameters used for each step of EST analysis

use "Quick Fast" Database scanner
 alignement further constrained to begin closer than 10bp to EST\5' end
 using BLOSUM62 substitution matrix

TABLE II

SEQ. ID		VON HEIJNE	TICCITE	DEFEDNAL
NO	CATEGORY	SCORE	TISSUE	INTERNAL
<u>110.</u>	CATEGORI	SCORE	SOURCE	DESIGNATION
ID38	new	10.8	Brain	33-19-2-H2-PU
ID39	new	10.8	Brain	33-56-1-E8-PU
ID40	new	10	Brain	33-79-3-D12-PU
ID41	new	9.6	Brain	33-72-2-B2-PU
ID42	new	9.5	Brain	33-13-2-B9-PU
ID43	new	9.1	Brain	33-113-1-E9-PU
ID44	new	9	Brain	33-28-4-E8-PU
ID45	new	8.8	Brain	33-12-3-F2-PU
ID46	new	8.8	Brain	33-70-1-C11-PU
ID47	new	8.5	Brain	33-74-1-B2-PU
ID48	new	8.5	Brain	33-29-3-F1-PU
ID49	new	8.4	Brain	33-8-2-A1-PU
ID50	new	8.3	Brain	17-17-3-A9-PU
ID51	new	8.3	Brain	33-106-2-A8-PU
ID52	new	8.3	Brain	
ID53	new	8.2	Brain	33-112-4-E7-PU 33-98-1-E6-PU
ID54	new	8.2		_
ID55			Brain	33-76-1-B6-PU
ID56	new	8	Brain	33-35-4-G8-PU
ID57	new	7.9	Brain	33-17-3-E4-PU
ID58	new	7.9	Brain	33-110-4-B5-PU
	new	7.8	Brain	33-40-1-A11-PU
ID59	new	7.7	Brain	33-71-1-A8-PU
ID60	new	7.7	Brain	33-96-3-G7-PU
ID61	new	7.6	Brain	33-112-3-D12-PU
ID62	new	7.6	Brain	33-62-2-B3-PU
ID63	new	7.6	Brain	33-6-4-G6-PU
ID64	new	7.5	Brain	33-82-4-E2-PU
ID65	new	7.4	Brain	33-81-3-H11-PU
ID66	new	7.3	Brain	33-64-1-B4-PU
ID67	new	7.2	Brain	33-31-1-B12-PU
ID68	new	7	Brain	33-24-4-F9-PU
ID69	new	7	Brain	33-110-3-E9-PU
ID70	new	7	Brain	33-4-2-G5-PU
ID71	new	6.9	Brain	33-74-2-A4-PU
ID72	new	6.9	Brain	33-52-4-F9-PU
ID73	new	6.9	Brain	33-74-1-B11-PU
ID74	new	6.8	Brain	33-10-4-D9-PU
ID75	new	6.8	Brain	33 <b>-</b> 15 <b>-</b> 2-H3-PU
ID76	new	6.7	Brain	33-38-2-D5-PU
ID77	new	6.7	Brain	33-78-3-D2-PU
ID78	new	6.7	Brain	33-96-3-D3-PU
ID79	new	6.6	Brain	33-76-4-B11-PU
ID80	new	6.3	Brain	33-39-1-C6-PU
ID81	new	6.1	Brain	33-106-3-B12-PU
ID82	new	6	Brain	33-4-2-B7-PU
ID83	new	5.9	Brain	33-99-2-E4-PU
ID84	new	5.9	Brain	33-34-1-B1-PU
ID85	new	5.8	Brain	33-67-4-E9-PU
ID86	new	5.7	Brain	33-11-3-H11-PU

SEQ. ID				
NO.	CATEGORY	VON HEIJNE	TISSUE	INTERNAL
	CATEGORI	SCORE	<b>SOURCE</b>	DESIGNATION
ID87	new	5.6		
ID88	new	5.6	Brain	33-13-2-A8-PU
ID89	пелу	5.6	Brain	33-83-4-B6-PU
ID90	new	5.6	Brain	33-70-1-E4-PU
ID91	new	5.6	Brain	33-5-3-H11-PU
ID92	new	5.5	Brain	33-10-3-G5-PU
ID93	пем	5.5	Brain	33-97-4-G4-PU
ID94	new	5.4	Brain Brain	33-46-4-F4-PU
ID95	new	5.3	Brain	33-4-1-G11-PU
ID96	new	5.3	Brain	33-105-1-H5-PU
ID97	new	5.3	Brain	33-74-2-B10-PU
ID98	new	5.3	Brain	33-49-3-E5-PU
ID99	new	5.2	Brain	33-114-2-A1-PU
ID100	new	5.2	Brain	33-71-1-G12-PU
ID101	new	5.2	Brain	33-47-3-E6-PU
ID102	new	5.2	Brain	33-1-2-E8-PU
ID103	new	5.1	Brain	33-93-4-E12-PU
ID104	new	5.1	Brain	33-1-2-H1-PU
ID105	new	5	Brain	17-10-1-H8-PU
ID106	new	5	Brain	33-110-2-B8-PU
ID107	new	5	Brain	33-104-3-D9-PU
ID108	new	4.9	Brain	33-72-2-H11-PU
ID109	new	4.9	Brain	33-7-4-D6-PU
ID110	new	4.9	Brain	33-31-4-G2-PU
ID111	new	4.8	Brain	33-109-1-E8-PU
ID112	new	4.8	Brain	17-1-2-B11-PU
ID113	new	4.8	Brain	33-19-4-H3-PU
ID114	new	4.8	Brain	33-14-4-E1-PU 33-70-3-H1-PU
ID115	new	4.7	Brain	33-86-4-H10-PU
ID116	new	4.7	Brain	33-107-3-D5-PU
ID117	new	4.7	Brain	33-23-4-B9-PU
ID118	new	4.7	Brain	33-82-4-H5-PU
ID119	new	4.6	Brain	33-16-3-F4-PU
ID120	new	4.6	Brain	33-97-4-C5-PU
ID121	new	4.6	Brain	33-100-3-B10-PU
ID122	new	4.6	Brain	33-59-3-E3-PU
ID123	пеw	4.5	Brain	33-25-1-G2-PU
ID124	new	4.5	Brain	17-16-3-B2-PU
ID125	new	4.4	Brain	33-52-4-E7-PU
ID126 ID127	new	4.4	Brain	33-91-1-D1-PU
	new	4.4	Brain	33-26-1-B9-PU
ID128 ID129	new	4.4	Brain	33-97-3-H6-PU
	new	4.4	Brain	33-109-2-E8-PU
ID130 ID131	new	4.3	Brain	33-59-2-B7-PU
	new	4.3	Brain	33-28-4-D1-PU
ID132	new	4.3	Brain	33-29-4-E2-PU
ID133	new	4.1	Brain	33-70-1-H6-PU
ID134 ID135	new	4.1	Brain	33-7-1-B2-PU
ID136	new	4.1	Brain	33-52-4-F8-PU
ID136	new	4.1	Brain	33-23-2-A6-PU
1010/	new	4.1	Brain	33-39-3-E5-PU

SEO ID	•	WOM THE TO THE		
SEQ. ID	CATECORY	VON HEIJNE	TISSUE	INTERNAL
NO.	CATEGORY	SCORE	SOURCE	DESIGNATION
ID138	new	4.1	Brain	33-81-4-H6-PU
ID139	new	4.1	Brain	33-105-3-F5-PU
ID140	new	4	Brain	33-35-2-H11-PU
ID141	new	4	Brain	33-50-3-E12-PU
ID142	new	4	Brain	
ID143	new	4		33-16-3-H7-PU
ID144	new	3.9	Brain	33-79-2-H4-PU
ID145	new	3.9	Brain	33-32-4-B12-PU
ID146	new	3.9	Brain	33-110-4-A5-PU
ID147	new	3.9	Brain	33-109-2-H1-PU
ID148	new	3.9	Brain	33-100-1-E6-PU
ID149	new	3.9	Brain	33-78-2-E7-PU
ID150	new	3.9	Brain	33-82-4-G3-PU
ID151	new	3.9	Brain	17-1-1-A9-PU
D152	new	3.9	Brain	33-89-4-E1-PU
ID152	new	3.9	Brain	33-89-1-B4-PU
ID155 ID154	new		Brain	33-96-3-A3-PU
ID155		3.8	Brain	33-92-3-D1-PU
ID156	new	3.8	Brain	33-104-4-H4-PU
ID150 ID157	new	3.8	Brain	33-106-1-B8-PU
	new	3.6	Brain	33-1-3-D1-PU
D158	new	3.6	Brain	33-40-2-F5-PU
ID159	new	3.6	Brain	33-4-1-E8-PU
D160	new	3.6	Brain	33-36-3-E2-PU
ID161	new	3.6	Brain	17-18-3-A6-PU
ID162	new	3.6	Brain	33-12-1-B1-PU
ID163	new	3.6	Brain	33-29-1-H1-PU
ID164	new	3.6	Brain	33-103-1-E1-PU
ID165	new	3.5	Brain	33-10-4-H2-PU
ID166	new	3.5	Brain	33-25-1-H2-PU
ID167	new	3.5	Brain	33-10-4-G2-PU
ID168	new	3.5	Brain	33-67-1-F4-PU
ID169	ext-est-not-vrt	12.5	Brain	33-77-4-E2-PU
ID170	ext-est-not-vrt	10.1	Brain	33-31-3-C11-PU
ID171	ext-est-not-vrt	9.8	Brain	33-28-2-H7-PU
ID172	ext-est-not-vrt	9.2	Brain	33-112-3-C8-PU
ID173	ext-est-not-vrt	7.9	Brain	33-23-3-A11-PU
ID174	ext-est-not-vrt	7.9	Brain	33-29-2-E11-PU
ID175	ext-est-not-vrt	7.9	Brain	33-66-4-C7-PU
ID176	ext-est-not-vrt	7.1	Brain	33-78-1-D7-PU
ID177	ext-est-not-vrt	6.6	Brain	33-31-3-D7-PU
ID178	ext-est-not-vrt	6.3	Brain	33-19-1-C11-PU
ID179	ext-est-not-vrt	6	Brain	33-67-1-A5-PU
ID180	ext-est-not-vrt	5.9	Brain	33-58-3-C8-PU
ID181	ext-est-not-vrt	4.9	Brain	33-107-4-C3-PU
ID182	ext-est-not-vrt	4.9	Brain	33-7-2-G12-PU
ID183	ext-est-not-vrt	4.8	Brain	33-11-1-G5-PU
ID184	ext-est-not-vrt	4.7	Brain	33-31-4-D9-PU
ID185	ext-est-not-vrt	4.6	Brain	33-26-4-E10-PU
ID186	ext-est-not-vrt	4.5	Brain	33-70-4-F7-PU
ID187	ext-est-not-vrt	4.5	Brain	33-19-2-D1-PU
ID188	ext-est-not-vrt	4.4	Brain	33-48-4-F8-PU
		•••	Diani	22-70-7-1:0-1:U

cco in				
SEQ. ID	CATECORY	VON HEIJNE	TISSUE	INTERNAL
NO.	CATEGORY	SCORE	SOURCE	DESIGNATION
ID189	ext-est-not-vrt	4.3	Brain	33-109-3-B10-PU
ID190	ext-est-not-vrt	4.1	Brain	33-30-2-A6-PU
ID191	ext-est-not-vrt	3.8	Brain	33-75-3-D7-PU
ID192	ext-est-not-vrt	3.7	Brain	33-109-4-C1-PU
ID193	est-not-ext	10.5	Brain	33-97-3-D4-PU
ID194	est-not-ext	10.1	Brain	33-61-2-F6-PU
ID195	est-not-ext	9.5	Brain	33-54-1-B9-PU
ID196	est-not-ext	9.3	Brain	33-39-1-D1-PU
ID197	est-not-ext	9.1	Brain	33-57-4-H5-PU
ID198	est-not-ext	9	Brain	33-60-2-B3-PU
ID199	est-not-ext	8.6	Brain	33-52-1-A1-PU
ID200	est-not-ext	8.4	Brain	33-82-2-H10-PU
ID201	est-not-ext	7.5	Brain	33-79-4-B11-PU
ID202	est-not-ext	7.5 7.5	Brain	
ID203	est-not-ext	7.5		33-18-3-H3-PU
ID204	est-not-ext	7.4 7.4	Brain Brain	33-21-1-D6-PU
ID204	est-not-ext	7.4		33-17-3-F9-PU
ID206	est-not-ext	7.4	Brain	33-70-2-G3-PU
ID207			Brain	33-89-3-H4-PU
ID208	est-not-ext	7.4	Brain	33-46-3-E10-PU
	est-not-ext	7	Brain	33-36-2-F9-PU
ID209	est-not-ext	6.8	Brain	33-39-1-C4-PU
ID210	est-not-ext	6.8	Brain	33-65-4-C6-PU
ID211	est-not-ext	6.4	Brain	33-18-2-G6-PU
ID212	est-not-ext	6.4	Brain	33-36-3-C6-PU
ID213	est-not-ext	6	Brain	33-79-2-B6-PU
ID214	est-not-ext	5.9	Brain	33-71-4-D11-PU
ID215	est-not-ext	5.9	Brain	17-12-2-A3-PU
ID216	est-not-ext	5.9	Brain	33-95-1-A12-PU
ID217	est-not-ext	5.8	Brain	33-5-3-E3-PU
ID218	est-not-ext	5.8	Brain	33-74-2-D3-PU
ID219	est-not-ext	5.7	Brain	33-50-3-H8-PU
ID220	est-not-ext	5.6	Brain	33-19-1-A2-PU
ID221	est-not-ext	5.5	Brain	33-22-1-D3 <b>-</b> PU
ID222	est-not-ext	5.5	Brain	33-97-1-G4-PU
ID223	est-not-ext	5.4	Brain	33-65-4-D10-PU
ID224	est-not-ext	5.4	Brain	33-79-4-C4-PU
ID225	est-not-ext	5.3	Brain	33-20-2-C5-PU
ID226	est-not-ext	5.2	Brain	33-34-4-A5-PU
ID227	est-not-ext	5.2	Brain	33-6-2-F11-PU
ID228	est-not-ext	5.2	Brain	33-2-2-G5-PU
ID229	est-not-ext	5.1	Brain	33-98-1-G7-PU
ID230	est-not-ext	5.1	Brain	33-20-3-B10-PU
ID231	est-not-ext	5	Brain	33-106-2-D9-PU
ID232	est-not-ext	4.9	Brain	33-72-2-A9-PU
ID233	est-not-ext	4.9	Brain	33-83-3-G8-PU
ID234	est-not-ext	4.8	Brain	33-31-3-E6-PU
ID235	est-not-ext	4.7	Brain	33-28-4-E2-PU
ID236	est-not-ext	4.6	Brain	33-101-3-F4-PU
ID237	est-not-ext	4.6	Brain	33-98-4-C1-PU
ID238	est-not-ext	4.5	Brain	33-31-2-E11-PU
ID239	est-not-ext	4 5	Brain	33-26-2-B6-PU
			Diam't	33 EO E-100-1 O

SEQ. ID		VON HEIJNE	TISSUE	INTERNAL
<u>NO</u>	CATEGORY	SCORE	SOURCE	DESIGNATION
<del></del>			0001100	<u>DEGIGNATION</u>
ID240	est-not-ext	4.4	Brain	33-75-4-H7-PU
ID241	est-not-ext	4.3	Brain	33-13-1-C6-PU
ID242	est-not-ext	4.3	Brain	33-35-4-G1-PU
ID243	est-not-ext	4.3	Brain	33-76-3-G11-PU
ID244	est-not-ext	4.2	Brain	33-72-1-A3-PU
ID245	est-not-ext	4.2	Brain	33-71-2-A2-PU
ID246	est-not-ext	4.2	Brain	33-23-3-H10-PU
ID247	est-not-ext	4.2	Brain	33-13-1-C1-PU
ID248	est-not-ext	4.2	Brain	33-43-2-G12-PU
ID249	est-not-ext	4.2	Brain	33-91-4-E10-PU
ID250	est-not-ext	4.1	Brain	33-113-2-B8-PU
ID251	est-not-ext	4	Brain	33-104-3-G9-PU
ID252	est-not-ext	3.9	Brain	33-66-2-B10-PU
ID253	est-not-ext	3.9	Brain	33-1-2-E9-PU
ID254	est-not-ext	3.9	Brain	33-51-1-G7-PU
ID255	est-not-ext	3.9	Brain	33-32-3-D11-PU
ID256	est-not-ext	3.8	Brain	33-43-2-H10-PU
ID257	est-not-ext	3.8	Brain	33-48-4-H11-PU
ID258	est-not-ext	3.8	Brain	33-8-4-C5-PU
ID259	est-not-ext	3.8	Brain	33-24-1-F5-PU
ID260	est-not-ext	3.8	Brain	33-70-1-A9-PU
ID261	est-not-ext	3.8	Brain	33-30-4-C4-PU
ID262	est-not-ext	3.8	Brain	33-10-2-G7-PU
ID263	est-not-ext	3.6	Brain	33-18-4-E12-PU
ID264	est-not-ext	3.6	Brain	33-52-1-G7-PU
ID265	est-not-ext	3.6	Brain	33-57-1-H10-PU
ID266	est-not-ext	3.5	Brain	33-80-3-E2-PU
ID267	est-not-ext	3.5	Brain	33-36-1-D3-PU
ID268	ext-vrt-not-genomic	11.3	Brain	33-101-1-A2-PU
ID269	ext-vrt-not-genomic	6.6	Brain	33-55-2-E8-PU
ID270	ext-vrt-not-genomic	4.8	Brain	33-14-2-H3-PU

### TABLE III

	TABLE III
SEQ. ID	
NO.	SIGNAL PEPTIDE
	- SAND TEATING
ID38	MLLLLGLCLGLSLC
ID39	MENGGAGTLQIRQVLLFFVLLGMSQA
ID40	MKGPEPGPOPTMEGDVI DTI EAT CARCONI -
	MRGPEPGPQPTMEGDVLDTLEALGYKGPLLEEQALTKAAEGGLSSPEFSELCIWLGSQIK SLCNLEESITSAGRDDLESFOLEISGFLKEMACPYSYLISCOMPRESSELCIWLGSQIK
	SLCNLEESITSAGRDDLESFQLEISGFLKEMACPYSVLISGDIKDRLKKKEDCLKLLLFL STELQA
ID41	MEKSWMLWNFVERWLIALASWSWALC
ID42	MQQTRTEAVAGAFSHCLGFCGMRLGLLLLARHWCIA
ID43	MEKGNAFLKNRL VVFLLLPLASGP
ID44	MFPFNQAGLPTLLMLIVFHAASMA
ID45	MTSRSLRRCSCI RVTHNYEU ACTUSI CURROLE
	MTSRSLRRCSCLRVTHNKEILASTVSLGVEGYMLGGGSRINSSNLNDGEEECSPDSLLVW KKKSLLLWMSSLPSLG
ID46	MWTASAMDFRTCIASYI PAL CYVICA CRAIN CONTRACTOR AND C
ID47	MWTASAMDFRTCIASXLPALCYVQACRALMIAASVLGLPAILLLLTVLPCIXM MGPPPTHIKYLHLNIYCNGKSTAPGIRSHSLGFALLSLSHPTCQA MFCLLTFLAFTTLLFA
ID48	MFCLLTFLAFTTLLFA
ID49	MHCGSTPGLCPCWVPFLKCLLAVLSSLFA
ID50	MNLVCSALLLLGIVSS
ID51	MSVLDDRQRDILVVQKRHSSLEAAMLIGLLAWLQT
ID52	MGVNGRRLLIICHYLPLSLC
ID53	MKLRECPALRWSOLSOHKLECLLL VLARGO
ID54	MIDPROILEAFPER()KTHADACCEUT AUTDDDEECH
	MDPRGILKAFPKRQKIHADASSKVLAKIPRREEGEEAEEWLSSLRAHVVRTGIGRARAEL FEKQIVQHGGQLCPAQGPGVTHIVVDEGMDYERALRLLRLPQLPPXCSA
ID55	MFWKLSLSLFLVAVLVKVAEA
ID56	MAFLGLFSLLVLQSMATG
ID57	MAFLGLFSLLVLOSMATG
ID58	MSFSLNFTLPANTTSSPVTGGVETDGGPGLGLGLGLG
ID59	MSTWYLALNKSYKNKDSVRIVI SI CTVSIVITIVI DIOTATALLVALLETLIHR
	MSTWYLALNKSYKNKDSVRIYLSLCTVSIKFTYFHDIQTNCLTTWKHSRCRFYWAFGGSI LQHSVDPLVLFLSLALLVTP
ID60	MAIGISLQLLCCIFTLYLO
ID61	MQATSNLLNLLLLSLFAGI.
ID62	MMK WKPEDLGS VPCEAFS VTI I CGWPGS HWC
ID63	MQATSNLLNLLLISUFAGI
ID64	MASSHWNETTTSVYOYI GFOVOK IVDEUDADA TEA CELTRA A TE
ID65	
ID66	MLFLQMGKOSWILIFFI NVTOI VPC
ID67	MELRXXPPGGREVOLLLGLCSppxxs1
ID68	MLWSLLSSSGSHFG
ID69	MDISGLIPGLVSTFILLSXSDHYGRKFPMILSSVGALATSVWLCLLCYFAFP
ID70	
ID71	MPVPACWISSSLSLLASHHSVSC
ID72	MCPVFSKOLLACGSLLPGLWO
ID73	MALTIHGERMRPDWESPWITSSQAQSLSLGGSPSSRGPLVPRGEYLASCPEGVRSHSHLL PRSLLPLSAWPPWAWH
1074	PRSLLPLSAWPPWAWH
ID74	MAARFRCGHLCVPEVPRGPASHAEGGGGRLSRKAAHQAQLCWRAGGDGRGNFN PMNFLVAGTFASSCHSPPLLWSLPPRILLASSLPTROUP
ID7s	PMNFLVAGTFASSCHSPPLLWSLPPRILIASSLPTLSHP
ID75	MASTISAT KEKMKET SVI STICGCEVTOR
ID76	MLUVYGKPVYOGHRSTI KKCDVI DENGRADA
ID77	KPKKMDSKMKHSVPVLPHGDQQYLFSPSREMPTFSGTLEGHLIPMAILLGQTQS MSVLEISGMIMNRVNSHIPGIGYOLGGNAVGLILGCTTTPLETTERS
וושו	MSVLEISGMIMNRVNSHIPGIGYQIFGNAVSLILGLTPFVFRLSQATDLEQLTAHSASEI. YVIAFGSNEDVIVLSMVIISFVVRVSI VWIEEFILGVA FRITZGODI I.
	YVIAFGSNEDVIVLSMVIISFVVRVSLVWIFFFLLCVAERTYKQRLLFAKLFGHLTSA
	1999 HEALT KONLLOHLISA

4714 F	
SEQ. ID	
<u>NO.</u>	SIGNAL PEPTIDE
ID 70	NOVOR/ ADDRODUL AND A STATE OF THE STATE OF
ID78	MCKGIKAGDTCEKLVGYSAVYRVCFGMACFFFIFCLLTLKINNSKSCRAHIHNGFWFFKL
TD 70	LLLGAMCSG
ID79	MSDSAGGRAGLRRYPKLPVWVVEDHQEVLPFIYRAIGSKHLPASNVSFLHFDSHPDLLIP
TD00	VNMPADTVFDKETLFGELSIENWIMPAVYAGHFSHVVWFHPTWA
ID80	MSSCRGQKVAGGLRVVSPFPLCQPAGEPSRGKMRSSCVLLTALVALA
ID81	MIIPFKIKNLGGRVLLSGREMFPASVRAPDLAVALSLLPAWT
ID82	MVCSAPRKIVVRAFITIIFIYYAIKKRANEPAAYLMLKPEALILLLLAQKGPS
ID83	MTESSMKKLASTLLDAITDKDPLVQEQVCSALCSLGEVRP
ID84	MQETDCNKRWGRGLGGLWSETGRRFHCKSFVFLFHCTSGLSSC
ID85	MLLEVPWLSSTVSCAQG
ID86	MSGGRMQARCSQQSTWSPAFLAVAGPGWA
ID87	MLQMLWHFLASFFPRAGC
ID88	MYSHPVSSLVCLLAMGKGLG
ID89	MGRKEEDDCSXWKKQTTNIRKTFIFMEVLGSGAFS
ID90	MMIAVFGNANDRNVLTLLPNQSLFSLARA
ID91	MFFELPLVVTAWFFGMCRS
ID92	MNHNIIICVMYIVPFLMTKCLYFCHSCKRGSFLLIVANVHFSQT
ID93	MSCGSAASLTGLCXCCLQALG
ID94	MQAVDNLTSAPGNTSLCTRDYKITQVLFPLLYTVLFFVGLITNGLA
ID95	MAAAMXLLCSSCCSWGPAAG
ID96	MDFIKDQSLSHRSVVKVLSLRKAQA
ID97	MTRPFWASCSTWATSRISCAFSLASSTA
ID98	MKSCAVSLTTAAVAFG
ID99	MSIHECACLSLSLICLRMSLS
ID100	MLSGLSFLSVFSLWC
ID101	MGLKDKSQAPASGLGVLRGQRSGSFISMPAPASGQXPEESRSPAPPVASRSQNRGYRPWH
	GPLWVHQSVRFGLYSILHFPFWVHG
ID102	MSDQIKFIMDSLNKEPFRKNYNLITFDSLEPMQLLQVLSDVLA
ID103	MSPSCLHPDLWSMCLEVPSFTATDSVNCGCCLELATEPARNIRSTTRASLLRCSSFTSTR
	NSTGISALPPAAPMAWPFSASLSTLPVPLTHSSVASLTATPSLA
ID104	MDLSFHLLLDPSSTQS
ID105	MPHFLDWFVXVYLVISVLILVGFGAC
ID106	MSKLKVIPEKSLTNNSRIVGLLAQLEKINA
ID107	MMSASRLAGTLIPAMAFLSCVRP
ID108	MVDGTQLRGLTRMYQVPLXLDRDETLVRLRFTMVALVTVCCXLVAFLFC
ID109	MKQNFLVLNSVWYLISMLOMLAVIIT
ID110	MECQNSSLKKCLLVEKSLVKASYLIAFQTAASKKPFSIAEELIKPYLVEMCLEVLGSSA
ID111	MHSSIKTKGSVMWLVALLEMCVC
ID112	MTVLPLEAISSLSSFVLG
ID113	MGTASRSNIARHLQTNLILFCVGAVGACTL
ID114	MNSSKEEMRELAALFYSVVVSTVSG
ID115	MSQDGGXGELKHMVMSFRVSELQVLLGFAGRNKSGRKHELLAKALHLLKSSC
ID116	MPCISLLGLLYNFVQVLCYLSIFCLGVLF
ID117	MKIAVLFCFFLLIIF
ID118	MAKQKPHVLGSRVMPASCVSERRRKPSFQVSTWSSASLRGSWQ
ID119	MGFLYLKSVFDVSLG
ID120	MRMGPGRKRDFSPVPWSQYFESMEDVEVENETGKDTFRVYKSGSEGPVLLLLHGGG
	HSALS
ID121	MIFLLYLLPSSEE
ID122	MRMGPGRKRDFSPVPWSQYFESMEDVEVENETGKDTFRVYKSGSEGPVLLLLHGGG
	HSALS

SEQ. ID	
NO.	SIGNAL PEPTIDE
ID123	MLSLLNLISILASIPS
ID124	MGTTSNMVTTIHLMLLWPVHPLLVG
ID125	MGDPERPEAAGLDQDERSSSDTNESEIKSNEEPLLRKSSRRFVIFPIQYPDIWKMYKQAQ
	ASFWTAEEVDLSKDLPHWNKLKADEKYFISHILAFFAASDG
ID126	MDAGLFSLLPHPPCVG
ID127	MLITLTYLIQGESA
ID128	MYTGFRIEATLLTRVQCLCAIPFAFS
ID129	MYKQAQASFWTAEEVDLSKDLPHWNKLKADEKYFISHILAFFAASDG
ID130	MLLHLCSVKNLYQNRFLGLAAMASPSRN
ID131	MPCPTWTCLKSFPSPTSS
ID132	MEDLFSPSIXPPAPNISVPILLGWGLNLTLGQG
ID133	MAETKDAAQMLVTFKDVAVTFTREEWRQLDLAQRTLYREVMLETCGLLVSLG
ID134	MLILSQNIAQLEA
ID135	MLLGASAQGLWAHSWTCSCSA
ID136	MAAPLELSCWGGGWG
ID137	MSXVGIDLGFLNCYIAVARS
ID138	MEYSKXFVVFSTMFTASSP
ID139	MPMASSPPPSPHPQEPAPLLPSLPRLSLPFRLPWASTATA
ID140	MQHVXGHXPDPIAIMYVCPPCGHTTWALGLKFLSSSSQ
ID141	MGWEMTCIKSFFWARSHAGFLKCLLLSSLQ
ID142	MVFGGVCPSVTSIIAESLQGWNLVQLSFAATTPVLA
ID143	MHFITWSLLFLYQCSL
ID144	MSGASPIERTPMEEAPSSCPTSSCWPSVASPSSSWS
ID145	MEWAGKQRDFQVRAAPGWDHLASFPGPSLRLFSGSQA
ID146	MIAFFDEDNPRKRRSYSFTQSAGILCQETTYSTPHTKLEKAKSPTADAKVVSLSLQTSSA
ID147	MGKSIXSLCSVXLKARLKGXLEAVHLCLRAQKRRTALFCTLPCPVERG
ID148	MCLHMTLFRVPFTFS
ID149	MLNILKTLTSAALP
ID150	MRARVWPRSHGIPVPSFLSKSSLSHTPSPLLCLYHPPVYT
ID151	MWNAVAIICNGSWCQTXSTSGLESLCLSLLIPGPKP
ID152	MLRLGLFKISWARC
ID153	MPFAEDKTYKYICRNFSNFCNVDVVEILPYLPCLTA
ID154	MPGSSGLRFICKSRNHPQFGSFSGTDSLSFLPPCPC
ID155	MDVTGDEEEEIKQEINMLKKYSHHRNIATYYGAFIKKNPPGMDDQLXLVMEFCGAGS
ID156	MIFGLYFVLAVKLFLVFLLNICKG
ID157	MRKKRVEELIVFPGEVTSFSSIKCSSWISSLASG
ID158	MPSSSLAELCLMQQDACLFSXFLAVSRH
ID159	MDLWSCLFPVMLMEPSKGLEDSEWKMALQMRMQLPCLVLG
ID160	MSGKGKCRPIALRRAVPLPTTSTLTSA
ID161	MTPKAIQKSSGLFCPSQA
ID162	MPDQFDQAVVLNQLRYSGMLETVRIRKAGYAVRRPFQDFYKRYKVLMRNLALPEDV
	RGKCTSLLQLYDASNS
ID163	MCLVSFFLELNVLQQ
ID164	MRSLACLTPCGHA
ID165	MHLLSNWANPASS
ID166	MWSGKWALVSPFAMLHSVWRLIPA
ID167	MKVHMHTKFCLICLLTFIFH
ID168	MGRRHWVLTHSALSLFYTADTSHG
ID169	MAVFVVLLALVAGVLG
ID170	MAPLLLQLAVLGAALA

SEQ. ID	
NO.	<u>SIĞNAL PEPTIDE</u>
ID171	MPVTVTRTTITTTTSSSGLGSPMIVGSPRALTQPLGLLRLLQLVSTCVA
ID172	MELVLVFLCSLLAPMVLA
ID173	MGPIWSSYYGNCRSLLFVMDASDPTQLSASCVQLLGLLSAEQLAEA
ID174	MSGGRAPAVLLGGVASLLLSFVWMPALLPVASRLLLLPRVLLTMASG
ID175	MALSCTLNRYLLLMAQEHLEFRLPEIXSLLLLFGGQFASS
ID176	MAARGVIAPVGESLRYAEYLQPSAKRPDADVDQQRLVRSLIAVGLGVAALAFA
ID177	MRMCAGSIYKSATQAVLGXLFLGGLCRG
ID178	MAERRRPLSPIPSXRRPSEPSRPRPAAAGXRSLPRPGDEELQLPCAVHDLIFWRDVKKTG
ID179	FVFGTTLIMLLSWQLSVS
шт	MAAPVLLRVSVPRWERVARYAVCAAGILLSIYAYHVEREKERDPEHRALCDLGPWVK
ID180	CSAALASRWGRGFGLLGSIFGKDGVLNQPNSVFGLIFYILQLLLGMTASAVA
ID180	MSFLQDPSFFTMGMWSIGAGALGAAALALLLANT MASLLCCGPKLAACGIVLSAWGVIMLIMLGIFFNVHS
ID182	MILPYRMXSLFLHAVSSSFT
ID183	
1103	MATLVELPDSVLLEIFSYLPVRDRIRISRVCHRWKRLVDDRWLWRHVDLTLYTVRALAGR AWA
ID184	
ID185	MKNACIVLPPTPPPSLQPSASLLAPNRFLFSCFCFLSHKFG
ID186	MAFGLQMFIQRKFPYPLQWSLLVAVVAG
ID187	MYCKILVLMLHTELIRTDYSSVDQLLLNYPAEEGLGRERSLLWTPLLSPGSLR
ID188	MAVSHSVKERTISENSLIILLQGLQG
ID189	MESGGRPSLCQFILLGTTSVVTA
ш109	MAALDLRAXWIRWSCSCLGXLXGAGGETNGVERPGGGGLALARQGSLRDGRQVGR
	APAVCFPHGAPGLPPRQRXXGGXPEVQGGESWCPRPRGGGASRTGLRRRKGPTKTPE PESSEAPQDPLNWFGILVPHSLRQAQA
ID190	MAFLPSPAWWISLLPSLLSIC
ID191	
ID191	MEPKVAELKQKIEDTLCPFGFEVYPFQVAWYNELLPPAFHLPLPGPTLA MLVLRSGLTKALA
ID192	
ID194	MSGGHLADLTLLFVLLLFSLLPA
ID195	MKPSRTPARLWMLPQQQAGAVVVAAPTERHPTHHMAGWLLGALTLLGLVTS
	MGESIPLAAPVPVEQAVLETFFSHLGIFSYDKAKDNVEKEREANKSAGGSWLSLLAALAH LAAA
ID196	MQMSYAIRCAFYQLLLAALMLVAMLQLLYLSLLSGLHG
ID197	MLRAELKIAVVLFAFHLLLSFILG
ID198	MNHQQTLIGRLLCDLHGLSLSPPVANNVQALFRMLTPEAYSCLLILLLRTFLCSA
ID199	MIITAVVSISVTIFCFQTKVDFTSCTGLFCVLGIVLLVTG
ID200	MAAGGRMEDGSLDITQSIEDDPLLDAQLLPHHSLQAHFRPRFHPLPTVIIVNLLWFIHLV FVVLX
ID201	MSPGCMLLFVFGFVGG
ID202	MKLLLGIALLAYVAS
ID203	MDILVPLLQLLVLLLTLPLHLMA
ID204	MEAASPSNSTGVERXADLMDADSLLLSLELASGSG
ID205	MIRQERSTSYQEAVRPALPSSKPCLLTSPAVLVKLLSSSASTS
ID206	MKLIDYGLSGYQEESAEVKAMDFITSTAILPLLFGCLGVFG
ID207	MRCLTTPMLLRALAQAARA
ID208	MSRFLNVLRSWLVMVSIIAMGNTLQSFRDHTFLYEKLYTGKPNLVNGLQARTFGIWTLLS
	SVIRCLC
ID209	MIFLTLSLDSRVSA
ID210	MQCFSFIKTMMILFNLLIFLCGAALLXVG
ID211	MAEAALEAVRXSYENSRPLQGSSACLLLCPTWTNP
ID212	MATASPSVFLLMVNGQVES
ID213	MAGIKALISLSFGGAIGLMFLMLGCALP

SEQ. ID NO.	SIGNAL PEPTIDE
ID214	MIGDILLFGTLLMNAGA
ID215	MKTMILTLSLFGSCIS
ID216	MDWRVPPSXXDPGHQDIPLPVTXXFISVSVLSSLGIVLA
ID217	MAAAALPAWLSLQSRA
ID218	MAMVSAMSWVLYLWISACAMLLCHG
ID219	MGKEWGWQEMENGGAAPAWGAGPPYHPAPPPVEKTLSWGCGFGLHSGFGGSGGG
	VGLCRLLCLVRLFCC
ID220	MLQTSNYSLVLSLQFLLLSYD
ID221	MWFEILPGLSVMGVCLLIPGLATA
ID222	MRPSPLSGILADPLXLFPFSEG
ID223	MRESLSXRSWHLPASLMMAQXFIPAVA
ID224	MSGVVPTAPEQPAXEMENQTKPPDPRPDAPPEYSSHXFTRTPWKQLSLHLLATRACYG
ID225	MWRYQFGWGVITRGPREIPFPPSLLASESLLPPLPDLVLTCTSLGFVTRVWMSLNLNELS
	LYSRTWVFTCLVFFCFG
ID226	MVKLLVAKILCMVGVFFFMLLGSLLPVKI
ID227	MPVSIMCLIGLKANASS
ID228	MKVILLYLVLEKLVSRA
ID229	MAVTLSLLLGGRVCXPSLA
ID230	MLNQTSGRTSLLPELGVVTPAQG
ID231	MTSENLVQTAPKKKNKGKKGLEPSQSTAAKVPKKAKTWIPEVHDQKADVSAWKDL
	FVPRPVLRALSFLGFSAPTPIQA
ID232	MAAFGRQXXXWHXLIPLTWACMA
ID233	MSLTSSPKKRRSICFDRFLMPQSQSGPSSLGESYRTGVGFLIPEGWFLSGCPHGSSA
ID234	MGELGNRSRCILFLSENPCLSESIFQSLXFCLSPPPSPS
ID235	MAELGLNEHHQNEVINYMRFARSKRGLRLKTVDSCFQDLKESRLVEDTFTIDEVSEVLNG
	LQAVVHSEVESELINTAYTNVLLLRQXFAQAEK
ID236	MVTLPSGTWAFSCPYLALVDGGMLGSAREDAHASVVSWAVGLLYAVAQG
[1237]	MASASARGNQDKDAHFPPPSKQSLLFCPKXXLHIHRAEISKIMRECOEESFWKRALPFSI.
	VSMLVTQG
ID238	MLLMKSILLKVVCVLCIYLKFKLMALIYVPDKNNTNNNILRYNHNEISIGISVQCHFILS
	LCVLCIVLT
ID239	MAQRLLLRRFLASVIS
ID240	MAASKVKQDMPPXGGYGPIDYKRNLPRRGLSGYSMLAIGIGTLIYGHWSIMKWNRERRRL
	QIEDFEARIALLPLLQA
ID241	MRHLVTEELFPCSNLEDVVEDNSHSYFTLRITMACKGVPSTLLSLAILSHISTP
ID242	MSAEVKVTGQNQEQFLLLAKSAKGAALATLIHQVLEAPGVYVFGELLDMPNVRELAESXF
	ASTFRLLXVFAYGTYA
ID243	MLLSIGMLMLSATQVXTILXVQLFAFLNLLPVEA
ID244	MGWEVVSLSYCGVSWG
ID245	MRECISVHVGQAGVQIGNACWELFCLEHGIQA
ID246	MAGPLQGGGARALDLLRGLPRVSLA
ID247	MPAGVPMSTYLKMFAASXLAMCAGA
ID248	MAVQCVRLARRSLPALALSLRASP
ID249	MFSIISRSRACSMYFKENAKPSQLRLMHHYLSTPTSA
ID250	MKRLLPATSLAGPVLS
ID251	MLIITNPWPKYFDAAGRLTPEFSQRLTNKIRELLQQMERGLKSADXXDGTGYTGWAGIAV
IDASA	LYLHLYDVFG
ID252	MCATETVRAWLAQGSSSAGWG
ID253 ID254	MLLLATHPETVGQVTLRVXPVSLEVSIQMCAAAAAAFCLKXXGANT
11/23+	MAASSATPAPXXSQRCGADAGSAARIVFRWGRGRRGARSPEGSGHHGRANSGLGGAQ LOGGAXG

SEQ. ID	
NO.	SIGNAL PEPTIDE
ID255	MLRRPLAGLAAAALGRA
ID256	MDRPGFVAALVAGGVAG
ID257	MIVWFEGISMDLLTLLFQRRS
ID258	MRTFVHFALDALMFPARRRA
ID259	MAAPPQLRALLVVVNALLRKRRYHAALAVLKGFRNGAVYGAKIRAPHALVMTFLFR
	NGSLQ
ID260	MPVDLGXALGLLPSLAKA
ID261	MNLFIMYMAGNTISIFPTMMVCMMAWRPIQALMAISATFKMLESSSQKFLQGLVYLIGNL
	MGLALAVYKCQS
ID262	MISLTDTQKIGMGLTGFGVFFLFFGMILFFDKALLAIGNVLFVAGLAFVIG
ID263	MAASGAPRILVDLLKLXVAPLAVFQMLKSMCAG
ID264	MASVSSATFSGHGARSLLQFLRLVGQ
ID265	MWYLAVLLVLFTLNIL
ID266	MFTFGRLFQIITVVTCLQFIQDCCIHSRQINSLLEXSSLSRC
ID267	MIQDRDRCAQAAAVAAVGNLEPRGTPGPEDEAFCLPGCVGTLCQLDWWIWG
ID268	MKIIFPILSNPVFRRTVKLLLCLLWIGYSQG
ID269	MVSRMVSTMLSGLLFWLASGWTPAFA
ID270	MTATLAAAADIATMVSGSSGLAXA

Minimum signal peptide score	false positive rate	false negative rate	proba(0.1)	proba(0.2)
6.5 7 7.5 8 8.5 9	0.05 0.04 0.033 0.025 0.021 0.015 0.012 0.009 0.007	0.304 0.368 0.418 0.512 0.581	0.467 0.519 0.565 0.615 0.659 0.694 0.725 0.763 0.78 0.816 0.836 0.856	0.664 0.708 0.745 0.782 0.813 0.836 0.855 0.878 0.889 0.909 0.92 0.93

TABLE IV

Minimum signal peptide score	All ESTs	New ESTs	ESTs matching public EST closer than 40 bp from beginning	- POOLING	ESTs extending public EST more than 40 bp
3.5	2674	947	599	23	150
4	2278	784	499	23	126
4.5	1943	647	425	22	112
5	1657	523	353	21	96
5.5		<b>1</b>	307	19	80
6	1190	1	238	18	68
6.5	1		186	18	60
7	893		161	15	48
7.5	l		132	12	36
8		1	101	11	29
8.5	4		83	8	26
9	1	1	63	_	24
9.5		1	48	6	18
10	303	47	35	6	15

**TABLE V** 

Tissue	All ESTs	New ESTs	ESTs matching public EST closer than 40 bp from beginning	ESTs extending known mRNA more than 40 bp	ESTs extending public EST more than 40 bp
Brain	329	131	75	3	24
Cancerous prostate	134	40	37	1	6
Cerebellum	17	9	1	0	6
Colon	21	11	4	0	0
Dystrophic muscle	41	18	8	0	1
Fetal brain	70	37	16	0	1
Fetal kidney	227	116	46	1	19
Fetal liver	13	7	2	0	o
Heart	30	15	7	0	1
Hypertrophic prostate	86	23	22	2	2
Kidney	10	7	3	0	
Large intestine	21	8	4	0	
Liver	23	9	6	0	o
Lung	24	12	4	0	
Lung (cells)	57	38	6	0	4
Lymph ganglia	163	60	23	2	12
Lymphocytes	23	6	4	0	
Muscle	33	16	6	0	
Normal prostate	181	61	45	7	li di
Ovary	90	57	12	1	
Pancreas	48	11	6	0	
Placenta	24	5	1	0	
Prostate	34	16	4	C	
Spleen	<b>5</b> 6	28	10	C	
Substantia nigra	108	47	27	. 1	6
Surrenals	15	3	3	1	· •
Testis	131	68	25	, 1	1
Thyroid	17	8	2	2 (	
Umbilical cord	55	17	12	2	1 3
Uterus	28	15	3	3 (	) 2
Non tissue-specific	568	48	177	7	2 28
Total	2677	947	601		

TABLE VI

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# Description of Transcription Factor Binding Sites present on promoters isolated from SignalTag sequences

Promoter sequence P13H2 (546 bp):

Matrix	Position	Orientation	Score	Longth	Sequence
CMYB_01	-502	•	0.983	9	TGTCAGTTG
MYOD_Q6	-501	-	0.961	10	CCCAACTGAC
S8_01	-444	•	0.960	11	AATAGAATTAG
S8_01	-425	•	0.966	11	AACTAAATTAG
DELTAEF1_01	-390	•	0.960	11	GCACACCTCAG
GATA_C	-364	•	0.964	11	AGATAAATCCA
CMYB_01	-349	•	0.958	9	CTTCAGTTG .
GATA1_02	-343	•	0.959	14	TTGTAGATAGGACA
GATA_C	-339	•	0.953	11	AGATAGGACAT
TAL1ALPHAE47_01	-235	+	0.973	16	CATAACAGATGGTAAG
TAL1BETAE47_01	-235	+	0.983	16	CATAACAGATGGTAAG
TAL1BETAITF2_01	<b>-2</b> 35	+	0.978	16	CATAACAGATGGTAAG
MYOD_Q6	-232	•	0.954	10	ACCATCTGTT
GATA1_04	-217	•	0.953	13	TCAAGATAAAGTA
IK1_01	-126	•	0.963	13	AGTTGGGAATTCC
IK2_01	-126	+	0.985	12	AGTTGGGAATTC
CREL_01	-123	+	0.962	10	TGGGAATTCC
GATA1_02	-96	+	0.950	14	TCAGTGATATGGCA
SRY_02	-41	•	0.951	12	TAAAACAAAACA
E2F_02	-33	+	0.957	8	TTTAGCGC
MZF1_01	-5	•	0.975	8	TGAGGGGA

### Promoter sequence P1684 (861bp):

Matrix	Position	Orientation	Score	Length	Sequence
NFY_Q6	-748	•	0.956	11	GGACCAATCAT
MZF1_01	-738	+	0.962	8	CCTGGGGA
CMYB_01	-684	+	0.994	9	TGACCGTTG
VMYB_02	-682	•	0.985	9	TCCAACGGT
STAT_01	-673	+	0.968	9	TTCCTGGAA
STAT_01	-673	-	0.951	9	TTCCAGGAA
MZF1_01	-556	•	0.956	8	TTGGGGGA
IK2_01	-451	+	0.965	12	GAATGGGATTTC
MZF1_01	-424	+	0.986	8	AGAGGGGA
SRY_02	-398	•	0.955	12	GAAAACAAAACA
MZF1_01	-216	•	0.960	8	GAAGGGGA
MYOD_Q6	-190	•	0.981	10	AGCATCTGCC
DELTAEF1_01	-176	+	0.958	11	TCCCACCTTCC
S8_01	5	•	0.992	11	GAGGCAATTAT
MZF1_01	16	•	0.986	8	AGAGGGGA

### Promoter sequence P29B6 (666 bp):

Matrix	Position	Orientation	Score	Length	Sequence
ARNT_01	-311	+	0.964	16	GGACTCACGTGCTGCT
NMYC_01	-309	•	0.965	12	ACTCACGTGCTG
USF_01	-309	+	0.985	12	ACTCACGTGCTG
USF_01	-309	•	0.985	12	CAGCACGTGAGT
NMYC_01	-309	•	0.956	12	CAGCACGTGAGT
MYCMAX_02	-309		0.972	12	CAGCACGTGAGT
USF_C	-307	•	0.997	8	TCACGTGC
USF_C	-307	-	0.991	8	GCACGTGA
MZF1_01	-292	-	0.968	8	CATGGGGA
ELK1_02	-105	+	0.963	14	CTCTCCGGAAGCCT
CETS1P54_01	-102	+	0.974	10	TCCGGAAGCC
AP1_Q4	-42	•	0.963	11	AGTGACTGAAC
AP1FJ_Q2	-42	•	0.961	11	AGTGACTGAAC
PADS_C	45	•	1.000	9	TGTGGTCTC

**TABLE VII** 

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### **CLAIMS**

- A purified or isolated nucleic acid comprising the sequence of one of SEQ ID
   NOs: 38-270 or comprising a sequence complementary thereto.
  - 2. The nucleic acid of Claim 1, wherein said nucleic acid is recombinant.
- 3. A purified or isolated nucleic acid comprising at least 10 consecutive bases of the sequence of one of SEQ ID NOs: 38-270 or one of the sequences complementary thereto.
- 4. A purified or isolated nucleic acid comprising at least 15 consecutive bases of one of the sequences of SEQ ID NOs: 38-270 or one of the sequences complementary thereto.
  - 5. The nucleic acid of Claim 4, wherein said nucleic acid is recombinant.
  - 6. A purified or isolated nucleic acid of at least 15 bases capable of hybridizing under stringent conditions to the sequence of one of SEQ ID NOs: 38-270 or one of the sequences complementary to the sequences of SEQ ID NOs: 38-270.
    - 7. The nucleic acid of Claim 6, wherein said nucleic acid is recombinant.
  - 8. A purified or isolated nucleic acid encoding a human gene product, said human gene product having a sequence partially encoded by one of the sequences of SEQ ID NO: 38-270.
- 9. A purified or isolated nucleic acid having the sequence of one of SEQ ID
   NOs: 38-270 or having a sequence complementary thereto.
  - A purified or isolated nucleic acid comprising the nucleotides of one of SEQ
     NOs: 38-270 which encode a signal peptide.
  - 11. A purified or isolated polypeptides comprising a signal peptide encoded by one of the sequences of SEQ ID NOs: 38-270.
  - 12. A vector encoding a fusion protein comprising a polypeptide and a signal peptide, said vector comprising a first nucleic acid encoding a signal peptide encoded by one of the sequences of SEQ ID NOs: 38-270 operably linked to a second nucleic acid encoding a polypeptide.
- 30 13. A method of directing the extracellular secretion of a polypeptide or the insertion of a polypetide into the membrane comprising the steps of:

obtaining a vector according to Claim 12; and

introducing said vector into a host cell such that said fusion protein is secreted into the extracellular environment of said host cell or inserted into the membrane of said host cell.

- 14. A method of importing a polypeptide into a cell comprising contacting said cell with a fusion protein comprising a signal peptide encoded by one of the sequences of SEQ ID NOs: 38-270 operably linked to said polypeptide.
- 15. A method of making a cDNA encoding a human secretory protein that is partially encoded by one of SEQ ID NOs 38-270, comprising the steps of:

obtaining a cDNA comprising one of the sequences of SEQ ID NOs: 38-270:

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contacting said cDNA with a detectable probe comprising at least 15 consecutive nucleotides of said sequence of SEQ ID NO: 38-270 or a sequence complementary thereto under conditions which permit said probe to hybridize to said cDNA;

identifying a cDNA which hybridizes to said detectable probe; and isolating said cDNA which hybridizes to said probe.

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- 16. An isolated or purified cDNA encoding a human secretory protein, said human secretory protein comprising the protein encoded by one of SEQ ID NOs 38-270 or a fragment thereof of at least 10 amino acids, said cDNA being obtainable by the method of Claim 15.
- 17. The cDNA of Claim 16 wherein said cDNA comprises the full protein coding sequence partially included in one of the sequences of SEQ ID NOs: 38-270.
- 18. A method of making a cDNA comprising one of the sequences of SEQ ID NOs: 38-270, comprising the steps of:

contacting a collection of mRNA molecules from human cells with a first primer capable of hybridizing to the polyA tail of said mRNA;

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hybridizing said first primer to said polyA tail;

reverse transcribing said mRNA to make a first cDNA strand;

making a second cDNA strand complementary to said first cDNA strand using at least one primer comprising at least 15 nucleotides of one of the sequences of SEQ ID NOs 38-270; and

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isolating the resulting cDNA comprising said first cDNA strand and said second cDNA strand.

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- 19: An isolated or purified cDNA encoding a human secretory protein, said human secretory protein comprising the protein encoded by one of SEQ ID NOs 38-270 or a fragment thereof of at least 10 amino acids, said cDNA being obtainable by the method of Claim 18.
- 5 20. The cDNA of Claim 19 wherein said cDNA comprises the full protein coding sequence partially included in one of the sequences of SEQ ID NOs: 38-270.
  - 21. The method of Claim 18, wherein the second cDNA strand is made by:

contacting said first cDNA strand with a first pair of primers, said first pair of primers comprising a second primer comprising at least 15 consecutive nucleotides of one of the sequences of SEQ ID NOs 38-270 and a third primer having a sequence therein which is included within the sequence of said first primer;

performing a first polymerase chain reaction with said first pair of nested primers to generate a first PCR product;

contacting said first PCR product with a second pair of primers, said second pair of primers comprising a fourth primer, said fourth primer comprising at least 15 consecutive nucleotides of said sequence of one of SEQ ID NO:s 38-270, and a fifth primer, said fourth and fifth primers being capable of hybridizing to sequences within said first PCR product; and

performing a second polymerase chain reaction, thereby generating a second PCR product.

- 22. An isolated or purified cDNA encoding a human secretory protein, said human secretory protein comprising the protein encoded by one of SEQ ID NOs 38-270, or a fragment thereof of at least 10 amino acids, said cDNA being obtainable by the method of Claim 21.
- 23. The cDNA of Claim 22 wherein said cDNA comprises the full protein coding sequence partially included in one of the sequences of SEQ ID NOs: 38-270.
  - 24. The method of Claim 18 wherein the second cDNA strand is made by: contacting said first cDNA strand with a second primer comprising at least 15 consecutive nucleotides of the sequences of SEQ ID NOs: 38-270;

hybridizing said second primer to said first strand cDNA; and extending said hybridized second primer to generate said second cDNA strand.

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- 25. An isolated or purified cDNA encoding a human secretory protein, said human secretory protein comprising the protein partially encoded by one of SEQ ID NOs 38-270 or comprising a fragment thereof of at least 10 amino acids, said cDNA being obtainable by the method of Claim 24.
- 5 26. The cDNA of Claim 25, wherein said cDNA comprises the full protein coding sequence partially included in of one of the sequences of SEQ ID NOs: 38-270.
  - 27. A method of making a protein comprising one of the sequences of SEQ ID NO: 271-503, comprising the steps of:

obtaining a cDNA encoding the full protein sequence partially included in one of the sequences of sequence of SEQ ID NO: 38-270;

inserting said cDNA in an expression vector such that said cDNA is operably linked to a promoter;

introducing said expression vector into a host cell whereby said host cell produces the protein encoded by said cDNA; and

isolating said protein.

- 28. An isolated protein obtainable by the method of Claim 27.
- 29. A method of obtaining a promoter DNA comprising the steps of: obtaining DNAs located upstream of the nucleic acids of SEQ ID NO: 38-270 or the sequences complementary thereto;
- screening said upstream DNAs to identify a promoter capable of directing transcription initiation; and

isolating said DNA comprising said identified promoter.

- 30. The method of Claim 29, wherein said obtaining step comprises chromosome walking from said nucleic acids of SEQ ID NO: 38-270 or sequences complementary thereto.
- The method of Claim 30, wherein said screening step comprises inserting said upstream sequences into a promoter reporter vector.
  - 32. The method of Claim 30, wherein said screening step comprises identifying motifs in said upstream DNAs which are transcription factor binding sites or transcription start sites.
- 30 An isolated promoter obtainable by the method of Claim 32.

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- 34. An isolated or purified protein comprising one of the sequences of SEQ ID NO: 271-503.
- 35. In an array of discrete ESTs or fragments thereof of at least 15 nucleotides in length, the improvement comprising inclusion in said array of at least one of the sequences of SEQ ID NOs: 38-270, or one of the sequences complementary to the sequences of SEQ ID NOs: 38-270, or a fragment thereof of at least 15 consecutive nucleotides.

- 36. The array of Claim 35 including therein at least two of the sequences of SEQ ID NOs: 38-270, the sequences complementary to the sequences of SEQ ID NOs: 38-270, or fragments thereof of at least 15 consecutive nucleotides.
- The array of Claim 35 including therein at least five of the sequences of SEQ ID NOs: 38-270, the sequences complementary to the sequences of SEQ ID NOs: 38-270, or fragments thereof of at least 15 consecutive nucleotides.

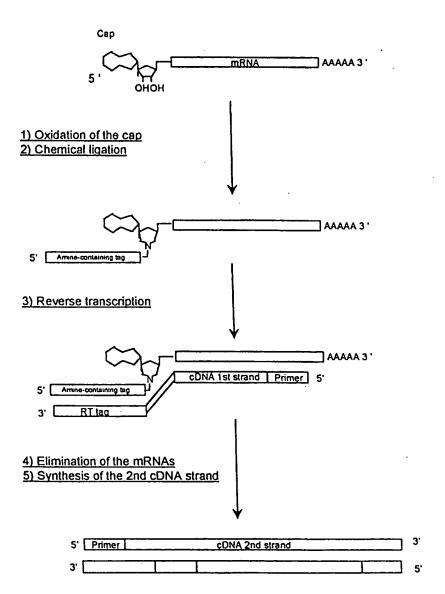
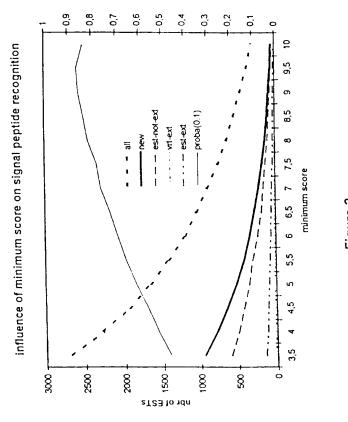


Figure 1



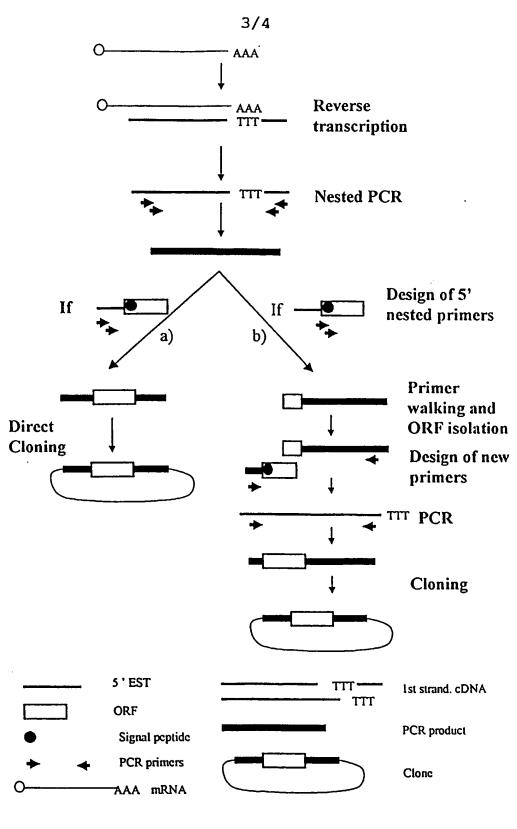
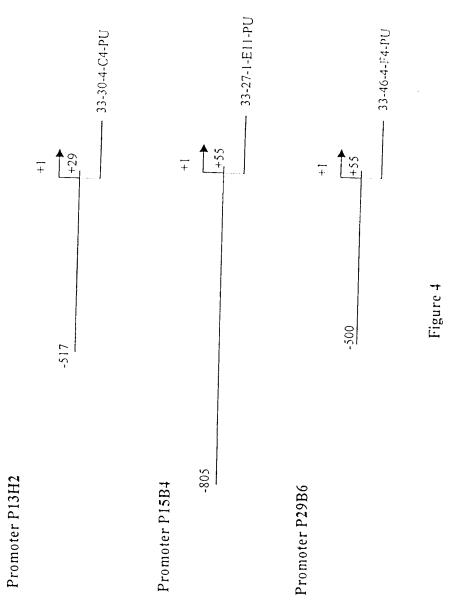


Figure 3



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SEQUENCE LISTING

```
(1) GENERAL INFORMATION:
        (i) APPLICANT:
           (A) NAME : GENSET SA
           (B) STREET :24, RUE ROYALE
           (C) CITY: PARIS
           (E) COUNTRY : FRANCE
           (F) POSTAL CODE (ZIP): 75008
      (ii) TITLE OF INVENTION: 5' EST FOR SECRETED PROTEINS EXPRESSED IN BRAIN
      (iii) NUMBER OF SEQUENCES: 503
      (v) COMPUTER READABLE FORM:
            (A) MEDIUM TYPE: Floppy Disk
            (B) COMPUTER: IBM PC compatible
           (C) OPERATING SYSTEM: Win95
           (D) SOFTWARE: Word
(2) INFORMATION FOR SEQ ID NO: 1:
      (i) SEQUENCE CHARACTERISTICS:
            (A) LENGTH: 47 base pairs
            (B) TYPE: NUCLEIC ACID
            (C) STRANDEDNESS: SINGLE
            (D) TOPOLOGY: LINEAR
      (ii) MOLECULE TYPE: Other nucleic acid
      (ix) FEATURE:
            (A) NAME/KEY: Cap
            (B) LOCATION: 1
            (D) OTHER INFORMATION: m7Gppp added to 1
      (x1) SEQUENCE DESCRIPTION: SEQ ID NO: 1:
GGCAUCCUAC UCCCAUCCAA UUCCACCCUA ACUCCUCCCA UCUCCAC
                                                                     47
(2) INFORMATION FOR SEQ ID NO: 2:
      : SEQUENCE CHARACTERISTICS:
            (A) LENGTH: 46 base pairs
            (B) TYPE: NUCLEIC ACID
            (C) STRANDEDNESS: SINGLE
            (D) TOPOLOGY: LINEAR
      (1.1) MOLECULE TYPE: Other nucleic acid
       (AL) SEQUENCE DESCRIPTION: SEQ ID NO: 2:
```

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(2)	INFORMATION FOR SEQ ID NO: 3:	
	(i) SEQUENCE CHARACTERISTICS:  (A) LENGTH: 25 base pairs  (B) TYPE: NUCLEIC ACID  (C) STRANDEDNESS: SINGLE  (D) TOPOLOGY: LINEAR	
	(ii) MOLECULE TYPE: Other nucleic acid	
	(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 3:	
ATC.	CAAGAATT CGCACGAGAC CATTA	25
(2)	INFORMATION FOR SEQ ID NO: 4:	·
	(i) SEQUENCE CHARACTERISTICS:  (A) LENGTH: 25 base pairs  (B) TYPE: NUCLEIC ACID  (C) STRANDEDNESS: SINGLE  (D) TOPOLOGY: LINEAR	·
	(ii) MOLECULE TYPE: Other nucleic acid	
	(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 4:	
TAA	ATGGTCTC GTGCGAATTC TTGAT	25
(2)	) INFORMATION FOR SEQ ID NO: 5:	
	<ul><li>(i) SEQUENCE CHARACTERISTICS:</li><li>(A) LENGTH: 25 base pairs</li><li>(B) TYPE: NUCLEIC ACID</li><li>(C) STRANDEDNESS: SINGLE</li><li>(D) TOPOLOGY: LINEAR</li></ul>	
	(ii) MOLECULE TYPE: Other nucleic acid	
	(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 5:	
ccc	GACAAGAC CAACGTCAAG GCCGC	25
(2)	) INFORMATION FOR SEQ ID NO: 6:	
	(i) SEQUENCE CHARACTERISTICS:  (A) LENGTH: 25 base pairs  (B) TYPE: NUCLEIC ACID  (C) STRANDEDNESS: SINGLE  (D) TOPOLOGY: LINEAR	

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(ii) MG	DLECULE TYPE: Other nucleic acid	
(xi) SI	EQUENCE DESCRIPTION: SEQ ID NO: 6:	
TCACCAGCAG G	CAGTGGCTT AGGAG	25
(2) INFORMAT	ION FOR SEQ ID NO: 7:	
	QUENCE CHARACTERISTICS: (A) LENGTH: 25 base pairs (B) TYPE: NUCLEIC ACID (C) STRANDEDNESS: SINGLE (D) TOPOLOGY: LINEAR	
(ii) Mo	OLECULE TYPE: Other nucleic acid	
(xi) S	EQUENCE DESCRIPTION: SEQ ID NO: 7:	
AGTGATTCCT G	CTACTTTGG ATGGC	25
(2) INFORMAT	ION FOR SEQ ID NO: 8:	
(i) SE	QUENCE CHARACTERISTICS: (A) LENGTH: 25 base pairs (B) TYPE: NUCLEIC ACID (C) STRANDEDNESS: SINGLE (D) TOPOLOGY: LINEAR	
(ii) M	OLECULE TYPE: Other nucleic acid	
(xi) S	EQUENCE DESCRIPTION: SEQ ID NO: 8:	
GCTTGGTCTT (	STTCTGGAGT TTAGA	25
(2) INFORMAT	TION FOR SEQ ID NO: 9:	
(i) SE	EQUENCE CHARACTERISTICS:  (A) LENGTH: 25 base pairs  (B) TYPE: NUCLEIC ACID  (C) STRANDEDNESS: SINGLE  (D) TOPOLOGY: LINEAR	
(ii) t	MOLECULE TYPE: Other nucleic acid	
(xi)	SEQUENCE DESCRIPTION: SEQ ID NO: 9:	

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TCCAGAATGG GAGACAAGCC AATTT

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WO 99/00552	FC1/1B36/0125

(2) INFORMATION FOR SEQ ID NO: 10:	
<ul> <li>(i) SEQUENCE CHARACTERISTICS:</li> <li>(A) LENGTH: 25 base pairs</li> <li>(B) TYPE: NUCLEIC ACID</li> <li>(C) STRANDEDNESS: SINGLE</li> <li>(D) TOPOLOGY: LINEAR</li> </ul>	
(ii) MOLECULE TYPE: Other nucleic acid	
(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 10:	
AGGGAGGAGG AAACAGCGTG AGTCC	25
(2) INFORMATION FOR SEQ ID NO: 11:	
<ul><li>(i) SEQUENCE CHARACTERISTICS:</li><li>(A) LENGTH: 25 base pairs</li><li>(B) TYPE: NUCLEIC ACID</li><li>(C) STRANDEDNESS: SINGLE</li><li>(D) TOPOLOGY: LINEAR</li></ul>	
(ii) MOLECULE TYPE: Other nucleic acid	
(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 11:	
ATGGGAAAGG AAAAGACTCA TATCA	25
(2) INFORMATION FOR SEQ ID NO: 12:	
(i) SEQUENCE CHARACTERISTICS:  (A) LENGTH: 25 base pairs  (B) TYPE: NUCLEIC ACID  (C) STRANDEDNESS: SINGLE  (D) TOPOLOGY: LINEAR	
(ii) MOLECULE TYPE: Other nucleic acid	
(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 12:	
AGCAGCAACA ATCAGGACAG CACAG	25
(2) INFORMATION FOR SEQ ID NO: 13:	
(i) SEQUENCE CHARACTERISTICS:  (A) LENGTH: 25 base pairs  (B) TYPE: NUCLEIC ACID  (C) STRANDEDNESS: SINGLE	

(D) TOPOLOGY: LINEAR

(ii) MOLECULE TYPE: Other nucleic acid

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ATCAAGAATT CGCACGAGAC CATTA 2
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(2)	INFORMATION	FOR SEC	OID :	NO: 14:
-----	-------------	---------	-------	---------

- (i) SEQUENCE CHARACTERISTICS:
  - (A) LENGTH: 67 base pairs
  - (B) TYPE: NUCLEIC ACID
  - (C) STRANDEDNESS: SINGLE
  - (D) TOPOLOGY: LINEAR
- (ii) MOLECULE TYPE: Other nucleic acid
- (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 14:

#### ATCGTTGAGA CTCGTACCAG CAGAGTCACG AGAGAGACTA CACGGTACTG GTTTTTTTTT 60

TTTTTVN 67

(2) INFORMATION FOR SEQ ID NO: 15:

- (i) SEQUENCE CHARACTERISTICS:
  - (A) LENGTH: 29 base pairs
  - (B) TYPE: NUCLEIC ACID
  - (C) STRANDEDNESS: SINGLE
  - (D) TOPOLOGY: LINEAR
- (ii) MOLECULE TYPE: Other nucleic acid
- (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 15:

CCAGCAGAGT CACGAGAGAG ACTACACGG

29

- (2) INFORMATION FOR SEQ ID NO: 16:
  - (i) SEQUENCE CHARACTERISTICS:
    - (A) LENGTH: 25 base pairs
    - (B) TYPE: NUCLEIC ACID
    - (C) STRANDEDNESS: SINGLE
    - (D) TOPOLOGY: LINEAR
  - (ii) MOLECULE TYPE: Other nucleic acid
  - (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 16:

CACGAGAGAG ACTACACGGT ACTGG

```
(i) SEQUENCE CHARACTERISTICS:
```

- (A) LENGTH: 526 base pairs
- (B) TYPE: NUCLEIC ACID
- (C) STRANDEDNESS: DOUBLE
- (D) TOPOLOGY: LINEAR

# (ii) MOLECULE TYPE: CDNA

#### (vi) ORIGINAL SOURCE:

- (A) ORGANISM: Homo Sapiens
- (F) TISSUE TYPE: Lymph ganglia

#### (ix) FEATURE:

- (A) NAME/KEY: other
- (B) LOCATION: complement(261..376)
- (C) IDENTIFICATION METHOD: blastn
- (D) OTHER INFORMATION: identity 96 region 166..281 id N70479

#### (ix) FEATURE:

- (A) NAME/KEY: other
- (3) LOCATION: complement(380..486)
- (C) IDENTIFICATION METHOD: blastn
- (D) OTHER INFORMATION: identity 97 region 54..160 id N70479

est

### (ix) FEATURE:

- (A) NAME/KEY: other
- (B) LOCATION: complement(110..145)
- (C) IDENTIFICATION METHOD: blastn
- (D) OTHER INFORMATION: identity 94

region 403..438

id N70479

est

# (ix) FEATURE:

- (A) NAME/KEY: other
- (B) LOCATION: complement(196..229)
- (C) IDENTIFICATION METHOD: blastn
- (D) OTHER INFORMATION: identity 94

region 315..348

id N70479

est

# (ix) FEATURE:

- (A) NAME/KEY: sig peptide
- (B) LOCATION: 90..140
- (C) IDENTIFICATION METHOD: Von Heijne matrix
- (D) OTHER INFORMATION: score 8.2

seq LLLITAILAVAVG/FP

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 17:

WO 99/06552		7		PCT/IB98/01236
GAGAGAAAGA ACTG	actgar acgitigac		GTT CTC CTC CTG Val Leu Leu Leu	
			GTC TCT CAA GAC Val Ser Gln Asp 5	
			GAA TTA GCT TCA Glu Leu Ala Ser 20	
			CCA CTT CCA CCA Pro Leu Pro Pro 35	
			TTT CCT ATT CCA Phe Pro Ile Pro	
	CCT ACA ACT CCC Pro Thr Thr Pro 60		GAA AAG TAAACAA Glu Lys	RAA 354
GGAAAAGTCA CRAT	AAACCT GGTCACCTC	GA AATTGAAATT	GAGCCACTTC CTTG.	AARAAT 414
CAAAATTCCT GTTA	ATAAAA RAAAAACA	a tgtaattgaa	ATAGCACACA GCAT	TCTCTA 474
GTCAATATCT TTAGTGATCT TCTTTAATAA ACATGAAAGC AAAAAAAAAA				
(2) INFORMATION FOR SEQ ID NO: 18:  (i) SEQUENCE CHARACTERISTICS:  (A) LENGTH: 17 amino acids  (B) TYPE: AMINO ACID  (D) TOPOLOGY: LINEAR				
(ii) MOLECULE TYPE: PROTEIN				
<pre>(vi) ORIGINAL SOURCE:    (A) ORGANISM: Homo Sapiens</pre>				
<pre>(ix) FEATURE:         (A) NAME/KEY: sig_peptide         (B) LOCATION: 117         (C) IDENTIFICATION METHOD: Von Heijne matrix         (D) OTHER INFORMATION: score 8.2</pre>				

Met Lys Lys Val Leu Leu Leu Ile Thr Ala Ile Leu Ala Val Ala Val I= 5 = 10 = 15

WO 99/06552

### (2) INFORMATION FOR SEQ ID NO: 19:

## (i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 822 base pairs
- (B) TYPE: NUCLEIC ACID
- (C) STRANDEDNESS: DOUBLE
- (D) TOPOLOGY: LINEAR

#### (ii) MOLECULE TYPE: CDNA

#### (vi) ORIGINAL SOURCE:

- (A) ORGANISM: Homo Sapiens
- (D) DEVELOPMENTAL STAGE: Fetal
- (F) TISSUE TYPE: kidney

#### (ix) FEATURE:

- (A) NAME/KEY: other
- (B) LOCATION: 260..464
- (C) IDENTIFICATION METHOD: blastn
- (D) OTHER INFORMATION: identity 96

region 153..357

id H57434

est

## (ix) FEATURE:

- (A) NAME/KEY: other
- (B) LOCATION: 118..184
- (C) IDENTIFICATION METHOD: blastn
- (D) OTHER INFORMATION: identity 98

region 98..164

id H57434

est

### (ix) FEATURE:

- (A) NAME/KEY: other
- (B) LOCATION: 56..113
- (C) IDENTIFICATION METHOD: blastn
- (D) OTHER INFORMATION: identity 98

region 35..92

id H57434

est

## (ix) FEATURE:

- (A) NAME/KEY: other
- (B) LOCATION: 454..485
- (C) IDENTIFICATION METHOD: blastn
- (D) OTHER INFORMATION: identity 100

region 348..379

id H57434

est

#### (ix) FEATURE:

- (A) NAME/KEY: other
- (B) LOCATION: 118..545
- (C) IDENTIFICATION METHOD: blastn
- (D) OTHER INFORMATION: identity 95

region 1..428

id N27248

est

# (ix) FEATURE:

WO 99/06552 PCT/IB98/01236

9 (A) NAME/KEY: other (B) LOCATION: 65..369 (C) IDENTIFICATION METHOD: blastn (D) OTHER INFORMATION: identity 98 region 41..345 id H94779 est (ix) FEATURE: (A) NAME/KEY: other (B) LOCATION: 61..399 (C) IDENTIFICATION METHOD: blastn (D) OTHER INFORMATION: identity 99 region 6..344 id H09880 est (ix) FEATURE: (A) NAME/KEY: other (B) LOCATION: 408..458 (C) IDENTIFICATION METHOD: blastn (D) OTHER INFORMATION: identity 92 region 355..405 id H09880 est (ix) FEATURE: (A) NAME/KEY: other (B) LOCATION: 60..399 (C) IDENTIFICATION METHOD: blastn (D) OTHER INFORMATION: identity 97 region 56..395 id H29351 est (ix) FEATURE: (A) NAME/KEY: other (B) LOCATION: 393..432 (C) IDENTIFICATION METHOD: blastn (D) OTHER INFORMATION: identity 90 region  $\overline{3}91..430$ id H29351 est (ix) FEATURE: (A) NAME/KEY: sig\_peptide (B) LOCATION: 346..408 (C) IDENTIFICATION METHOD: Von Heijne matrix (D) OTHER INFORMATION: score 5.5 seq SFLPSALVIWTSA/AF (M1) SEQUENCE DESCRIPTION: SEQ ID NO: 19: ACTECTTTTA GCATAGGGGC TTCGGCGCCA GCGGCCAGCG CTAGTCGGTC TGGTAAGTGC 60 CTGATGCCGA GTTCCGTCTC TCGCGTCTTT TCCTGGTCCC AGGCAAAGCG GASGNAGATC 120 CTCAAACGGC CTAGTGCTTC GCGCTTCCGG AGAAAATCAG CGCTCTAATT AATTCCTCTG 180

GTTTGTTGAA GCAGTTACCA AGAATCTTCA ACCCTTTCC: ACAARAGCTA ATTGAGTACA

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CGTTCCTGTT GAGTACACGT TCCTGTTGAT TTACAAAAGG	TGCAGGTATG AGCAGGTCTG 300
AAGACTAACA TTTTGTGAAG TTGTAAAACA GAAAACCTGT	TAGAA ATG TGG TGG TTT 357  Met Trp Trp Phe  -20
CAG CAA GGC CTC AGT TTC CTT CCT TCA GCC CTT Gln Gln Gly Leu Ser Phe Leu Pro Ser Ala Leu -15 -10	
GCT GCT TTC ATA TTT TCA TAC ATT ACT GCA GTA Ala Ala Phe Ile Phe Ser Tyr Ile Thr Ala Val 1, 5 10	
GAC CCG GCT TTA CCT TAT ATC AGT GAC ACT GGT Asp Pro Ala Leu Pro Tyr Ile Ser Asp Thr Gly 20 25	
AAA TGC TTA TTT GGG GCA ATG CTA AAT ATT GCG Lys Cys Leu Phe Gly Ala Met Leu Asn Ile Ala 35 40	
AAA TAGAAATCAG GAARATAATT CAACTTAAAG AAKTTC Lys	ATTT CATGACCAAA 602
CTCTTCARAA ACATGTCTTT ACAAGCATAT CTCTTGTATT	GCTTTCTACA CTGTTGAATT 662
GTCTGGCAAT ATTTCTGCAG TGGAAAATTT GATTTARMTA	GTTCTTGACT GATAAATATG 722
GTAAGGTGGG CTTTTCCCCC TGTGTAATTG GCTACTATGT	CTTACTGAGC CAAGTTGTAW 782
TTTGAAATAA AATGATATGA GAGTGACACA AAAAAAAAAA	822

- (2) INFORMATION FOR SEQ ID NO: 20:
  - (i) SEQUENCE CHARACTERISTICS:
    - (A) LENGTH: 21 amino acids
    - (B) TYPE: AMINO ACID
    - (D) TOPOLOGY: LINEAR
  - (ii) MOLECULE TYPE: PROTEIN
  - (vi) ORIGINAL SOURCE:
    - (A) ORGANISM: Homo Sapiens
  - (ix) FEATURE:
    - (A) NAME/KEY: sig\_peptide
    - (B) LOCATION: 1..21
    - (C) IDENTIFICATION METHOD: Von Heijne matrix
    - (D) OTHER INFORMATION: score 5.5

seq SFLPSALVIWTSA/AF

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 20:

Met Trp Trp Phe Gln Gln Gly Leu Ser Phe Leu Pro Ser Ala Leu Val 1 5 15 Ile Trp Thr Ser Ala 20

(2) INFORMATION FOR SEQ ID NO: 21:
<ul> <li>(i) SEQUENCE CHARACTERISTICS:</li> <li>(A) LENGTH: 405 base pairs</li> <li>(B) TYPE: NUCLEIC ACID</li> <li>(C) STRANDEDNESS: DOUBLE</li> <li>(D) TOPOLOGY: LINEAR</li> </ul>
(ii) MOLECULE TYPE: CDNA
<pre>(vi) ORIGINAL SOURCE:     (A) ORGANISM: Homo Sapiens     (F) TISSUE TYPE: Testis</pre>
<pre>(ix) FEATURE:     (A) NAME/KEY: other     (B) LOCATION: complement(103398)     (C) IDENTIFICATION METHOD: blastn     (D) OTHER INFORMATION: identity 96</pre>
<pre>(ix) FEATURE:     (A) NAME/KEY: sig_peptide     (B) LOCATION: 185295     (C) IDENTIFICATION METHOD: Von Heijne matrix     (D) OTHER INFORMATION: score 5.9</pre>
(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 21:
ATCACCTTCT TCTCCATCCT TSTCTGGGCC AGTCCCCARC CCAGTCCCTC TCCTGACCTG 6
CCCAGCCCAA GTCAGCCTTC AGCACGCGCT TTTCTGCACA CAGATATTCC AGGCCTACCT 12
GGCATTCCAG GACCTCCGMA ATGATGCTCC AGTCCCTTAC AAGCGCTTCC TGGATGAGGG 18
TGGC ATG GTG CTG ACC ACC CTC CCC TTG CCC TCT GCC AAC AGC CCT GTG  Met Val Leu Thr Thr Leu Pro Leu Pro Ser Ala Asn Ser Pro Val  -35  -30  -25
AAC ATG CCC ACC ACT GGC CCC AAC AGC CTG AGT TAT GCT AGC TCT GCC Asn Met Pro Thr Thr Gly Pro Asn Ser Leu Ser Tyr Ala Ser Ser Ala -20 -15 -10
CTG TCC CCC TGT CTG ACC GCT CCA AAK TCC CCC CGG CTT GCT ATG ATG Leu Ser Pro Cys Leu Thr Ala Pro Xaa Ser Pro Arg Leu Ala Met Met -5 1 5 10
CCT GAC AAC TAAATATCCT TATCCAAATC AATAAARWRA RAATCCTCCC TCCARAAGGG 380 Pro Asp Asn

405

(2) INFORMATION FOR SEQ ID NO: 22:

- (i) SEQUENCE CHARACTERISTICS:
  - (A) LENGTH: 37 amino acids
  - (B) TYPE: AMINO ACID
  - (D) TOPOLOGY: LINEAR
- (ii) MOLECULE TYPE: PROTEIN
- (vi) ORIGINAL SOURCE:
  - (A) ORGANISM: Homo Sapiens
- (ix) FEATURE:
  - (A) NAME/KEY: sig\_peptide
  - (B) LOCATION: 1..37
  - (C) IDENTIFICATION METHOD: Von Heijne matrix
  - (D) OTHER INFORMATION: score 5.9

seq LSYASSALSPCLT/AP

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 22:

Met Val Leu Thr Thr Leu Pro Leu Pro Ser Ala Asn Ser Pro Val Asn 1 5 10 15

Met Pro Thr Thr Gly Pro Asn Ser Leu Ser Tyr Ala Ser Ser Ala Leu 20 25 30

Ser Pro Cys Leu Thr 35

- (2) INFORMATION FOR SEQ ID NO: 23:
  - (i) SEQUENCE CHARACTERISTICS:
    - (A) LENGTH: 496 base pairs
    - (B) TYPE: NUCLEIC ACID
    - (C) STRANDEDNESS: DOUBLE
    - (D) TOPOLOGY: LINEAR
  - (ii) MOLECULE TYPE: CDNA
  - (vi) ORIGINAL SOURCE:
    - (A) ORGANISM: Homo Sapiens
    - (F) TISSUE TYPE: Cancerous prostate
  - (ix) FEATURE:
    - (A) NAME/KEY: other
    - (B) LOCATION: 149..331
    - (C) IDENTIFICATION METHOD: blastn
    - (D) OTHER INFORMATION: identity 98 region 1..183 id AA397994 est
  - (ix) FEATURE:

PCT/IB98/01236 WO 99/06552

WO 99/06552	PCT/IB98/0123
(A) NAME/KEY: other (B) LOCATION: 328485 (C) IDENTIFICATION METHO (D) OTHER INFORMATION:	OD: idlastn identity 96 region 179336 id AA397994 est
<pre>(ix) FEATURE:     (A) NAME/KEY: other     (B) LOCATION: complement     (C) IDENTIFICATION METHO     (D) OTHER INFORMATION:</pre>	
(ix) FEATURE:  (A) NAME/KEY: sig_peptic  (B) LOCATION: 196240  (C) IDENTIFICATION METHO  (D) OTHER INFORMATION:	
(xi) SEQUENCE DESCRIPTION: SE	Q ID NO: 23:
RARAAATTGG TCCCAGTTTT CACCCTGCCG CA	AGGGCTGGC TGGGGAGGGC AGCGGTTTAG . 60
ATTAGCCGTG GCCTAGGCCG TTTAACGGGG TG	SACACGAGO NTGCAGGGCC GAGTCCAAGG 120
CCCGGAGATA GGACCAACCG TCAGGAATGC GA	AGGAATGTT TTTCTTCGGA CTCTATCGAG 180
GCACACAGAC AGACC ATG GGG ATT CTG TC Met Gly Ile Leu Se -15	TT ACA GTG ACA GCC TTA ACA TTT 231 er Thr Val Thr Ala Leu Thr Phe -10 -5
GCC ARA GCC CTG GAC GGC TGC AGA AAT Ala Xaa Ala Leu Asp Gly Cys Arg Asn 1 5	
GAG AAG CAC AGA CTC GAG AAA TGT AGG Glu Lys His Arg Leu Glu Lys Cys Arg 15 20	
GCC CCA GGA TCA ACC CAS CAC CGA AGA Ala Pro Gly Ser Thr Xaa His Arg Arg 30	
TCT TCA GCC TGAAATGAAK CCGGGATCAA <i>I</i> Ser Sor Ala	ATGGTTGCTG ATCARAGCCC ATATTTAAAT 434
TGGARLAGTC AANTTGASCA TTATTAAATA AA	ASCETUTIT AATATGTCTC AAACAAAAAA 494
ia,	496

(i) SEQUENCE CHARACTERISTICS:  (A) LENGTH: 15 amino acids  (B) TYPE: AMINO ACID  (D) TOPOLOGY: LINEAR	
(ii) MOLECULE TYPE: PROTEIN	
(vi) ORIGINAL SOURCE: (A) ORGANISM: Homo Sapiens	
<pre>(ix) FEATURE:     (A) NAME/KEY: sig_peptide     (B) LOCATION: 115     (C) IDENTIFICATION METHOD: Von Heijne matrix     (D) OTHER INFORMATION: score 5.5</pre>	
(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 24:	
Met Gly Ile Leu Ser Thr Val Thr Ala Leu Thr Phe Ala Xaa Ala 1 5 10 15	
(2) INFORMATION FOR SEQ ID NO: 25:	
<ul> <li>(i) SEQUENCE CHARACTERISTICS:</li> <li>(A) LENGTH: 623 base pairs</li> <li>(B) TYPE: NUCLEIC ACID</li> <li>(C) STRANDEDNESS: DOUBLE</li> <li>(D) TOPOLOGY: LINEAR</li> </ul>	
(ii) MOLECULE TYPE: CDNA	
<pre>(vi) ORIGINAL SOURCE:    (A) ORGANISM: Homo Sapiens    (F) TISSUE TYPE: Testis</pre>	
<pre>(ix) FEATURE:     (A) NAME/KEY: sig_peptide     (B) LOCATION: 4996     (C) IDENTIFICATION METHOD: Von Heijne matrix     (D) OTHER INFORMATION: score 10.1</pre>	
(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 25:	
AAAGATCCCT GCAGCCCGGC AGGAGAGAAG GCTGAGCCTT CTGGCGTC ATG GAG AGG Met Glu Arg -15	57
CTC GTC CTA ACC CTG TGC ACC CTC CCG CTG GCT GTG GCG TCT GCT GGC Leu Val Leu Thr Leu Cys Thr Leu Pro Leu Ala Val Ala Ser Ala Gly -10 -5 1	105
TGC GCC ACG ACG CCA GCT CGC AAC CTG AGC TGC TAC CAG TGC TTC AAG Cys Ala Thr Thr Pro Ala Arg Asn Leu Ser Cys Tyr Gln Cys Phe Lys	153

W	O 99.	/06552	2						15						PCT/IB9	8/01236
GTC Val 20	AGC Ser	AGC Ser	TGG Trp	ACG Thr	GAG Glu 25	TGC Cys	CCG Pro	CCC Pro	ACC Thr	TGG Trp 30	TGC Cys	AGC Ser	CCG Pro	CTG Leu	GAC Asp 35	201
						GAG Glu										249
						CGC Arg										297
						CCG Pro										345
						GCT Ala 90										393
						CRA Xaa										441
						GTG Val										489
						CTC Leu										534
TAA	CACT	GTG (	GGTG	cccc	CA C	CTGT	GCAT'	r GG	GACC	ACRA	CTT	CACC	CTC '	TTGG.	ARACAA	594
TAA	ACTC'	TCA '	TGCC	CCCA	AA AA	AAAA	AAAA									623

# (2) INFORMATION FOR SEQ ID NO: 26:

- (i) SEQUENCE CHARACTERISTICS:
  - (A) LENGTH: 16 amino acids
  - (B) TYPE: AMINO ACID
  - (D) TOPOLOGY: LINEAR
- (ii) MOLECULE TYPE: PROTEIN
- (vi) ORIGINAL SOURCE:
  - (A) ORGANISM: Homo Sapiens
- (ix) FEATURE:
  - (A) NAME/KEY: sig\_peptide
  - (B) LOCATION:  $1..\overline{16}$
  - (C) IDENTIFICATION METHOD: Von Heijne matrix
  - (D) OTHER INFORMATION: score 10.1

504 LVLTLCTLPLAVA/SA

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 26:

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		16	
1	5	10	15

(2)	INFORMATION	FOR	SEQ	ID	NO:	27:
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(i)	SEQUENCE	CHARACTERISTICS:
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- (A) LENGTH: 848 base pairs
- (B) TYPE: NUCLEIC ACID
- (C) STRANDEDNESS: DOUBLE
- (D) TOPOLOGY: LINEAR

# (ii) MOLECULE TYPE: CDNA

## (vi) ORIGINAL SOURCE:

- (A) ORGANISM: Homo Sapiens
- (D) DEVELOPMENTAL STAGE: Fetal
- (F) TISSUE TYPE: kidney

# (ix) FEATURE:

- (A) NAME/KEY: sig\_peptide (B) LOCATION: 32..73
- (C) IDENTIFICATION METHOD: Von Heijne matrix
- (D) OTHER INFORMATION: score 10.7

seq LWLLFFLVTAIHA/EL

# (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 27:

AACTTTGCCT TGT	TGTTTTCC ACCCTG	TG TGG CTG CTC T eu Trp Leu Leu P -10	
		CCA GGT GCA GAA Pro Gly Ala Glu 5	
		CTG GGA GAT AAA Leu Gly Asp Lys	
	hr Asn Glu Glu	AAA GCG ATG GTA Lys Ala Met Val 40	
		ACA GAA ATT TCC Thr Glu Ile Ser 55	
		TTC TGG TTT GTG Phe Trp Phe Val 70	
		GTT GAG GTG CAA Val Glu Val Gln 85	
		GCC TTC TTT CTA Ala Phe Phe Leu	

,	WO 99	9/0655	52						1	7					PCT/IB9	8/0123
													CCA Pro 120			439
													ATA Ile			487
													ATC Ile			535
													GCT Ala		<del>-</del>	583
													TCT Ser			631
													ACA Thr 200			679
	AGG Arg					TGA	AGGG	CTG '	rtgt'	rctg(	CT T	CCTC.	AARA.	A		727
ATT	AAAC	TTA	TGTT'	TCTG	TG T	GACT(	GCTG.	A GC.	ATCC'	TGAA	ATA	CCAA	GAG (	CAGA'	rca <b>t</b> at	787
WTT	TTGT	TTC	ACCA'	TTCT	TC T	TTTG	TAAT.	a aa	TTTT	GAAT	GTG	CTTG	AAA .	AAAA	AAAAA	847
С																848

## (2) INFORMATION FOR SEQ ID NO: 28:

- (i) SEQUENCE CHARACTERISTICS:
  - (A) LENGTH: 14 amino acids
  - (B) TYPE: AMINO ACID
  - (D) TOPOLOGY: LINEAR
- (ii) MOLECULE TYPE: PROTEIN
- (vi) ORIGINAL SOURCE:
  - (A) ORGANISM: Homo Sapiens
- (ix) FEATURE:
  - (A) MAME/KEY: sig\_poptide (B) LOCATION: 1..14

  - (C) IDENTIFICATION METHOD: Von Heijne matrix
  - (D) OTHER INFORMATION: score 10.7 seq LWLLFFLVTAIHA/EL
- (X1) SEQUENCE DESCRIPTION: (AQ ID NO: 28:

Met Leu Trp Leu Leu Phe Phe Leu 7.1 Thr Ala Ile His Ala 1 5 10

18

```
(2) INFORMATION FOR SEQ ID NO: 29:
      (i) SEQUENCE CHARACTERISTICS:
            (A) LENGTH: 25 base pairs
            (B) TYPE: NUCLEIC ACID
            (C) STRANDEDNESS: SINGLE
            (D) TOPOLOGY: LINEAR
      (ii) MOLECULE TYPE: Other nucleic acid
      (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 29:
GGGAAGATGG AGATAGTATT GCCTG
                                                                     25
(2) INFORMATION FOR SEQ ID NO: 30:
      (i) SEQUENCE CHARACTERISTICS:
            (A) LENGTH: 26 base pairs
            (B) TYPE: NUCLEIC ACID
            (C) STRANDEDNESS: SINGLE
            (D) TOPOLOGY: LINEAR
      (ii) MOLECULE TYPE: Other nucleic acid
      (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 30:
CTGCCATGTA CATGATAGAG AGATTC
                                                                     26
(2) INFORMATION FOR SEQ ID NO: 31:
      (i) SEQUENCE CHARACTERISTICS:
            (A) LENGTH: 546 base pairs
            (B) TYPE: NUCLEIC ACID
            (C) STRANDEDNESS: DOUBLE
            (D) TOPOLOGY: LINEAR
      (ii) MOLECULE TYPE: Genomic DNA
      (ix) FEATURE:
            (A) NAME/KEY: promoter
            (B) LOCATION: 1..517
      (ix) FEATURE:
```

(A) NAME/KEY: transcription start site

(D) OTHER INFORMATION: name CMYB 01

(C) IDENTIFICATION METHOD: matinspector prediction

score 0.983

sequence TGTCAGTTG

(A) NAME/KEY: TF binding-site

(B) LOCATION: 518

(B) LOCATION: 17..25

(ix) FEATURE:

```
(ix) FEATURE:
        (A) NAME/KEY: TF binding-site
        (B) LOCATION: complement (18..27)
       (C) IDENTIFICATION METHOD: matinspector prediction
       (D) OTHER INFORMATION: name MYOD_Q6
                                score 0.961
                                sequence CCCAACTGAC
 (ix) FEATURE:
       (A) NAME/KEY: TF binding-site
       (B) LOCATION: complement (75..85)
       (C) IDENTIFICATION METHOD: matinspector prediction
       (D) OTHER INFORMATION: name S8_01
                                score 0.960
                                sequence AATAGAATTAG
 (ix) FEATURE:
       (A) NAME/KEY: TF binding-site
       (B) LOCATION: 94..104
       (C) IDENTIFICATION METHOD: matinspector prediction
       (D) OTHER INFORMATION: name S8_01
                               score 0.966
                               sequence AACTAAATTAG
(ix) FEATURE:
      (A) NAME/KEY: TF binding-site
      (B) LOCATION: complement(129..139)
      (C) IDENTIFICATION METHOD: matinspector prediction
      (D) OTHER INFORMATION: name DELTAEF1_01
                               score 0.960
                               sequence GCACACCTCAG
(ix) FEATURE:
      (A) NAME/KEY: TF binding-site
      (B) LOCATION: complement(155..165)
      (C) IDENTIFICATION METHOD: matinspector prediction
      (D) OTHER INFORMATION: name GATA_C
                               score 0.9\overline{64}
                               sequence AGATAAATCCA
(ix) FEATURE:
      (A) NAME/KEY: TF binding-site
      (B) LOCATION: 170..178
      (C) IDENTIFICATION METHOD: matinspector prediction
      (D) OTHER INFORMATION: name CMYB_01
                               score 0.9\overline{5}8
                               sequence CTTCAGTTG
(ix) FEATURE:
     (A) NAME/KEY: TF binding-site
      (B) LOCATION: 176..189
      (C) IDENTIFICATION METHOD: matinspector prediction
      (D) OTHER INFORMATION: name GATA1 02
                              score 0.959
                               sequence TTGTAGATAGGACA
(ix) FEATURE:
     (A) NAME/KEY: TF binding-site
     (3) LOCATION: 180..190
     (C) IDENTIFICATION METHOD: matinspector prediction
```

(D) OTHER INFORMATION: name GATA\_C score 0.953 sequence AGATAGGACAT

(ix) FEATURE:

(A) NAME/KEY: TF binding-site

(B) LOCATION: 284..299

(C) IDENTIFICATION METHOD: matinspector prediction

(D) OTHER INFORMATION: name TALIALPHAE47 01

score 0.973

sequence CATAACAGATGGTAAG

(ix) FEATURE:

(A) NAME/KEY: TF binding-site

(B) LOCATION: 284..299

(C) IDENTIFICATION METHOD: matinspector prediction

(D) OTHER INFORMATION: name TAL1BETAE47\_01 score 0.983

sequence CATAACAGATGGTAAG

(ix) FEATURE:

(A) NAME/KEY: TF binding-site

(B) LOCATION: 284..299

(C) IDENTIFICATION METHOD: matinspector prediction

(D) OTHER INFORMATION: name TAL1BETAITF2\_01

score 0.978

sequence CATAACAGATGGTAAG

(ix) FEATURE:

(A) NAME/KEY: TF binding-site

(B) LOCATION: complement (287..296)

(C) IDENTIFICATION METHOD: matinspector prediction

(D) OTHER INFORMATION: name MYOD\_Q6 score 0.954

score 0.954
sequence ACCATCTGTT

(ix) FEATURE:

(A) NAME/KEY: TF binding-site

(3) LOCATION: complement(302..314)

(C) IDENTIFICATION METHOD: matinspector prediction

(D) OTHER INFORMATION: name GATA1\_04

score 0.953

sequence TCAAGATAAAGTA

(ix) FEATURE:

(A) NAME/KEY: TF binding-site

(B) LOCATION: 393..405

(C) IDENTIFICATION METHOD: matinspector prediction

(D) OTHER INFORMATION: name IK1 01

score  $0.\overline{9}63$ 

sequence AGTTGGGAATTCC

(ix) FEATURE:

(A) NAME/KEY: TF binding-site

(B) LOCATION: 393..404

(C) IDENTIFICATION METHOD: matinspector prediction

D) OTHER INFORMATION: name IK2\_01

score  $0.\overline{9}85$ 

sequence AGTTGGGAATTC

(ix) FEATURE:

WO 99/06552 21 PCT/IB98/01236

(A) NAME/KEY: TF binding-site (B) LOCATION: 396405 (C) IDENTIFICATION METHOD: matinspector prediction (D) OTHER INFORMATION: name CREL_01 score 0.962 sequence TGGGAATTCC	
(ix) FEATURE:  (A) NAME/KEY: TF binding-site  (B) LOCATION: 423436	
(C) IDENTIFICATION METHOD: matinspector prediction (D) OTHER INFORMATION: name GATA1 02 score 0.950 sequence TCAGTGATATGGCA	
(ix) FEATURE:  (A) NAME/KEY: TF binding-site  (B) LOCATION: complement (478489)  (C) IDENTIFICATION METHOD: matinspector prediction  (D) OTHER INFORMATION: name SRY 02  score 0.951  sequence TAAAAACAAAACA	
(ix) FEATURE:  (A) NAME/KEY: TF binding-site  (B) LOCATION: 486493  (C) IDENTIFICATION METHOD: matinspector prediction  (D) OTHER INFORMATION: name E2F 02  score 0.957  sequence TTTAGCGC	
<pre>(ix) FEATURE:     (A) NAME/KEY: TF binding-site     (B) LOCATION: complement(514521)     (C) IDENTIFICATION METHOD: matinspector prediction     (D) OTHER INFORMATION: name MZF1_01</pre>	
(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 31:	
TGAGTGCAGT GTTACATGTC AGTTGGGTTA AGTTTGTTAA TGTCATTCAA ATCTTCTATG	60
TCTTGATTTG CCTGCTAATT CTATTATTTC TGGAACTAAA TTAGTTTGAT GGTTCTATTA	60 120
TCTTGATTTG CCTGCTAATT CTATTATTTC TGGAACTAAA TTAGTTTGAT GGTTCTATTA GTTATTGACT GAGGTGTGCT AATCTCCCAT TATGTGGATT TATCTATTTC TTCAGTTGTA	120 180
TCTTGATTTG CCTGCTAATT CTATTATTTC TGGAACTAAA TTAGTTTGAT GGTTCTATTA GTTATTGACT GAGGTGTGCT AATCTCCCAT TATGTGGATT TATCTATTTC TTCAGTTGTA GATAGGACAT TGATAGATAC ATAAGTACCA GGACAAAAGC AGGGAGATCT TTTTTCCAAA	120 180
TCTTGATTTG CCTGCTAATT CTATTATTTC TGGAACTAAA TTAGTTTGAT GGTTCTATTA GTTATTGACT GAGGTGTGCT AATCTCCCAT TATGTGGATT TATCTATTTC TTCAGTTGTA GATAGGACAT TGATAGATAC ATAAGTACCA GGACAAAAGC AGGGAGATCT TTTTTCCAAA ATCAGGAGAA AAAATGACA TCTGGAAAAC CTATAGGGAA AGGCATAACA GATGGTAAGG	120 180 240 300
TCTTGATTTG CCTGCTAATT CTATTATTTC TGGAACTAAA TTAGTTTGAT GGTTCTATTA GTTATTGACT GAGGTGGCT AATCTCCCAT TATGTGGATT TATCTATTTC TTCAGTTGTA GATAGGACAT TGATAGATAC ATAAGTACCA GGACAAAAGC AGGGAGATCT TTTTTCCAAA ATCAGGAGAA AAAATGACA TCTGGAAAAC CTATAGGGAA AGGCATAACA GATGGTAAGG	120 180 240 300
TCTTGATTTG CCTGCTAATT CTATTATTTC TGGAACTAAA TTAGTTTGAT GGTTCTATTAGTTTGATTGATTGATTGATTGATTGATTGA	120 180 240 300
TCTTGATTTG CCTGCTAATT CTATTATTTC TGGAACTAAA TTAGTTTGAT GGTTCTATTAA GTTATTGACT GAGGTGTGCT AATCTCCCAT TATGTGGATT TATCTATTTC TCAGGTTGTA GATAGGACAT TGATAGATAC ATAAGTACCA GGACAAAAGC AGGGAGATCT TTTTTCCAAA ATCAGGAGAA AAAAATGACA TCTGGAAAAAC CTATAGGGAA AGGCATAACA GATGGTAAGG ATACTTTATC TTGAGTAGGA GAGCCTTCCT GTGGCAACGT GGAGAAGGGA AGAGGTCGTA GAATTGAGGA GTCAGCTCAG TTAGAACCAG GGAGTTGGGA ATTCCGTTCA TGTGATTTAG CATCAGTGAT ATGGCAAATG TGGGACTAAG GGTAGTGAT AGAGGGTTAA AATTGTGTGT	120 180 240 300 360
TCTTGATTTG CCTGCTAATT CTATTATTTC TGGAACTAAA TTAGTTTGAT GGTTCTATTAGTTTGATTGATTGATTGATTGATTGATTGA	120 180 240 300 360 420

```
(2) INFORMATION FOR SEQ ID NO: 32:
```

- (i) SEQUENCE CHARACTERISTICS:
  - (A) LENGTH: 23 base pairs
  - (B) TYPE: NUCLEIC ACID
  - (C) STRANDEDNESS: SINGLE
  - (D) TOPOLOGY: LINEAR
- (ii) MOLECULE TYPE: Other nucleic acid
- (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 32:

## GTACCAGGGA CTGTGACCAT TGC

23

- (2) INFORMATION FOR SEQ ID NO: 33:
  - (i) SEQUENCE CHARACTERISTICS:
    - (A) LENGTH: 24 base pairs
    - (B) TYPE: NUCLEIC ACID
    - (C) STRANDEDNESS: SINGLE
    - (D) TOPOLOGY: LINEAR
  - (ii) MOLECULE TYPE: Other nucleic acid
  - (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 33:

## CTGTGACCAT TGCTCCCAAG AGAG

24

- (2) INFORMATION FOR SEQ ID NO: 34:
  - (i) SEQUENCE CHARACTERISTICS:
    - (A) LENGTH: 861 base pairs
    - (B) TYPE: NUCLEIC ACID
    - (C) STRANDEDNESS: DOUBLE
    - (D) TOPOLOGY: LINEAR
  - (ii) MOLECULE TYPE: Genomic DNA
  - (ix) FEATURE:
    - (A) NAME/KEY: promoter
    - (B) LOCATION: 1..806
  - (ix) FEATURE:
    - (A) NAME/KEY: transcription start site
    - (B) LOCATION: 807
  - (ix) FEATURE:
    - (A) NAME/KEY: TF binding-site
    - (B) LOCATION: complement(60..70)
    - (C) IDENTIFICATION METHOD: matinspector prediction
    - (D) OTHER INFORMATION: name NFY\_Q6 score 0.956

```
sequence GGACCAATCAT
 (ix) FEATURE:
       (A) NAME/KEY: TF binding-site
       (B) LOCATION: 70..77
       (C) IDENTIFICATION METHOD: matinspector prediction
       (D) OTHER INFORMATION: name MZF1_01
                                score 0.9\overline{6}2
                                sequence CCTGGGGA
 (ix) FEATURE:
       (A) NAME/KEY: TF binding-site
       (B) LOCATION: 124..132
       (C) IDENTIFICATION METHOD: matinspector prediction
       (D) OTHER INFORMATION: name CMYB 01
                               score 0.994
                               sequence TGACCGTTG
 (ix) FEATURE:
       (A) NAME/KEY: TF binding-site
      (B) LOCATION: complement(126..134)
      (C) IDENTIFICATION METHOD: matinspector prediction
      (D) OTHER INFORMATION: name VMYB 02
                               score 0.985
                               sequence TCCAACGGT
(ix) FEATURE:
      (A) NAME/KEY: TF binding-site
      (B) LOCATION: 135..143
      (C) IDENTIFICATION METHOD: matinspector prediction
      (D) OTHER INFORMATION: name STAT 01
                               score 0.968
                               sequence TTCCTGGAA
(im) FEATURE:
      (A) NAME/KEY: TF binding-site
      (B) LOCATION: complement(135..143)
      (C) IDENTIFICATION METHOD: matinspector prediction
      (D) OTHER INFORMATION: name STAT 01
                              score 0.951
                              sequence TTCCAGGAA
(ix) FEATURE:
      (A) NAME/KEY: TF binding-site
      (B) LOCATION: complement(252..259)
      (C) IDENTIFICATION METHOD: matinspector prediction
      (D) OTHER INFORMATION: name MZF1 01
                              score 0.956
                              sequence TTGGGGGA
(ix) FEATURE:
      (A) NAME/KEY: TF binding-site
      (B) LOCATION: 357..368
     (C) IDENTIFICATION METHOD: matinspector prediction
     (D) OTHER INFORMATION: name IK2_01
                              score 0.965
                              sequence GAATGGGATTTC
(LE) FEATURE:
```

(A) NAME/KEY: TF binding-site(B) LOCATION: 334...391

(C) IDENTIFICATION METHOD: matinspector prediction (D) OTHER INFORMATION: name MZF1 01 score 0.986 sequence AGAGGGGA (ix) FEATURE: (A) NAME/KEY: TF binding-site (B) LOCATION: complement (410..421) (C) IDENTIFICATION METHOD: matinspector prediction (D) OTHER INFORMATION: name SRY 02 score  $0.\overline{955}$ sequence GAAAACAAAACA (ix) FEATURE: (A) NAME/KEY: TF binding-site (B) LOCATION: 592..599 (C) IDENTIFICATION METHOD: matinspector prediction (D) OTHER INFORMATION: name MZF1 01 score  $0.9\overline{60}$ sequence GAAGGGGA (ix) FEATURE: (A) NAME/KEY: TF binding-site (B) LOCATION: 618..627 (C) IDENTIFICATION METHOD: matinspector prediction (D) OTHER INFORMATION: name MYOD Q6 score 0.981 sequence AGCATCTGCC (ix) FEATURE: (A) NAME/KEY: TF binding-site (B) LOCATION: 632..642 (C) IDENTIFICATION METHOD: matinspector prediction (D) OTHER INFORMATION: name DELTAEF1 01 score 0.958 sequence TCCCACCTTCC (ix) FEATURE: (A) NAME/KEY: TF binding-site (B) LOCATION: complement (813..823) (C) IDENTIFICATION METHOD: matinspector prediction (D) OTHER INFORMATION: name S8 01 score 0.992 sequence GAGGCAATTAT (ix) FEATURE: (A) NAME/KEY: TF binding-site (B) LOCATION: complement (824..831) (C) IDENTIFICATION METHOD: matinspector prediction (D) OTHER INFORMATION: name MZF1 01 score 0.986 sequence AGAGGGGA (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 34: TACTATAGGG CACGCGTGGT CGACGGCCGG GCTGTTCTGG AGCAGAGGGC ATGTCAGTAA 60

TGATTGGTCC CTGGGGAAGG TCTGGCTGGC TCCAGCACAG TGAGGCATTT AGGTATCTCT

CTCAGAGGGC	TAGGCACGAG	GGAAGGTCAG	AGGAGAAGGS	AGGSARGGCC	CAGTGAGARG	240
					TGGGMACTTR	300
	CCAASCAGAA					360
GGGATTTCAG	GTTAGNCAGG	GTGAGAGGGG	AGGCTCTCTG	GCTTAGTTTT	GTTTTGTTTT	420
	GTAACTTGCT					480
	CCCTACCACT					540
	GAGAACATGG					600
	CCCAAAGAGC					660
	GTTTGGACAA					720
	ATACCTAGGC					780
CCTGATGGT	CCTTTAGGTT	TGGGCACAAA	ATATAATTGC	CTCTCCCCTC	TCCCATTTTC	840
CTCTTGGGA	GCAATGGTCA	С				861

# (2) INFORMATION FOR SEQ ID NO: 35:

- (i) SEQUENCE CHARACTERISTICS:
  - (A) LENGTH: 20 base pairs

  - (B) TYPE: NUCLEIC ACID
    (C) STRANDEDNESS: SINGLE
  - (D) TOPOLOGY: LINEAR
- (ii) MOLECULE TYPE: Other nucleic acid
- (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 35:

CTGGGATGGA AGGCACGGTA 20

# (2) INFORMATION FOR SEQ ID NO: 36:

- (i) SEQUENCE CHARACTERISTICS:
  - (A) LENGTH: 20 base pairs
  - (B) TYPE: NUCLEIC ACID
  - (C) STRANDEDNESS: SINGLE
  - (D) TOPOLOGY: LINEAR
- (ii) MOLECULE TYDE: Other nucleic acid
- (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 36:

#### (2) INFORMATION FOR SEQ ID NO: 37:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 555 base pairs

(B) TYPE: NUCLEIC ACID

(C) STRANDEDNESS: DOUBLE

(D) TOPOLOGY: LINEAR

(ii) MOLECULE TYPE: Genomic DNA

(ix) FEATURE:

(A) NAME/KEY: promoter(B) LOCATION: 1..500

(ix) FEATURE:

(A) NAME/KEY: transcription start site

(B) LOCATION: 501

(ix) FEATURE:

(A) NAME/KEY: TF binding-site

(B) LOCATION: 191..206

(C) IDENTIFICATION METHOD: matinspector prediction

(D) OTHER INFORMATION: name ARNT\_01 score 0.964

sequence GGACTCACGTGCTGCT

(ix) FEATURE:

(A) NAME/KEY: TF binding-site

(B) LOCATION: 193..204

(C) IDENTIFICATION METHOD: matinspector prediction

(D) OTHER INFORMATION: name NMYC\_01 score 0.965

sequence ACTCACGTGCTG

(ix) FEATURE:

(A) NAME/KEY: TF binding-site

(B) LOCATION: 193..204

(C) IDENTIFICATION METHOD: matinspector prediction

(D) OTHER INFORMATION: name USF\_01 score 0.985

sequence ACTCACGTGCTG

(ix) FEATURE:

(A) NAME/KEY: TF binding-site

(B) LOCATION: complement(193..204)

(C) IDENTIFICATION METHOD: matinspector prediction

(D) OTHER INFORMATION: name USF\_01
score 0.985
sequence CAGCACGTGAGT

(ix) FEATURE:

(A) NAME/KEY: TF binding-site

(B) LOCATION: complement (193..204)

(C) IDENTIFICATION METHOD: matinspector prediction

(D) OTHER INFORMATION: name NMYC\_01 score 0.956 sequence CAGCACGTGAGT

(ix) FEATURE:

(A) NAME/KEY: TF binding-site

(B) LOCATION: complement (193..204)

(C) IDENTIFICATION METHOD: matinspector prediction

(D) OTHER INFORMATION: name MYCMAX\_02 score 0.972

sequence CAGCACGTGAGT

#### (ix) FEATURE:

- (A) NAME/KEY: TF binding-site
- (B) LOCATION: 195..202
- (C) IDENTIFICATION METHOD: matinspector prediction
- (D) OTHER INFORMATION: name USF\_C score 0.997 sequence TCACGTGC

## (ix) FEATURE:

- (A) NAME/KEY: TF binding-site
- (B) LOCATION: complement(195..202)
- (C) IDENTIFICATION METHOD: matinspector prediction
- (D) OTHER INFORMATION: name USF\_C score 0.991 sequence GCACGTGA

#### (ix) FEATURE:

- (A) NAME/KEY: TF binding-site
- (3) LOCATION: complement(210..217)
- (C) IDENTIFICATION METHOD: matinspector prediction
- (D) OTHER INFORMATION: name MZF1\_01 score 0.968 sequence CATGGGGA

#### (ix) FEATURE:

- (A) NAME/KEY: TF binding-site
- (B) LOCATION: 397..410
- (C) IDENTIFICATION METHOD: matinspector prediction
- (D) OTHER INFORMATION: name ELK1\_02
  score 0.963
  sequence CTCTCCGGAAGCCT

#### (ix) FEATURE:

- (A) NAME/KEY: TF binding-site
- (B) LOCATION: 400..409
- (C) IDENTIFICATION METHOD: matinspector prediction
- (D) OTHER INFORMATION: name CETS1P54\_01 score 0.974 sequence TCCGGAAGCC

#### (ix) FEATURE:

- (A) NAME/KEY: TF binding-site
- (B) LOCATION: complement(460..470)
- ( $\mathbb{C}$ ) IDENTIFICATION METHOD: matinspector prediction
- (D) OTHER INFORMATION: name API\_Q4
  score 0.963
  sequence AGTGACTGAAC

# (1X) FEATURE:

- (A) NAME/KEY: TF binding-site
- (B) LOCATION: complement (460..470)
- (C) IDENTIFICATION METHOD: matinspector prediction
- (D) OTHER INFORMATION: name APIFJ Q2 score 0.961 sequence AGTGACTGAAC

WO 99/06552	28	PCT/IB98/01236
(ix) FEATURE:	TF hinding-site	

(C) IDENTIFICATION METHOD: matinspector prediction

(D) OTHER INFORMATION: name PADS\_C score 1.000 sequence TGTGGTCTC

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 37:

(B) LOCATION: 547..555

CTATAGGGCA CGCKTGGTCG ACGGCCCGGG CTGGTCTGGT CTGTKGTGGA GTCGGGTTGA 60 AGGACAGCAT TTGTKACATC TGGTCTACTG CACCTTCCCT CTGCCGTGCA CTTGGCCTTT 120 KAWAAGCTCA GCACCGGTGC CCATCACAGG GCCGGCAGCA CACACATCCC ATTACTCAGA AGGAACTGAC GGACTCACGT GCTGCTCCGT CCCCATGAGC TCAGTGGACC TGTCTATGTA GAGCAGTCAG ACAGTGCCTG GGATAGAGTG AGAGTTCAGC CAGTAAATCC AAGTGATTGT 300 CATTCCTGTC TGCATTAGTA ACTCCCAACC TAGATGTGAA AACTTAGTTC TTTCTCATAG 360 GTTGCTCTGC CCATGGTCCC ACTGCAGACC CAGGCACTCT CCGGAAGCCT GGAAATCACC 420 CGTGTCTTCT GCCTGCTCCC GCTCACATCC CACACTTGTG TTCAGTCACT GAGTTACAGA 480 TTTTGCCTCC TCAATTTCTC TTGTCTTAGT CCCATCCTCT GTTCCCCTGG CCAGTTTGTC 540 TAGCTGTGTG GTCTC 555

## (2) INFORMATION FOR SEQ ID NO: 38:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 155 base pairs(B) TYPE: NUCLEIC ACID(C) STRANDEDNESS: DOUBLE

(D) TOPOLOGY: LINEAR

(ii) MOLECULE TYPE: CDNA

(vi) ORIGINAL SOURCE:

(A) ORGANISM: Homo Sapiens
(F) TISSUE TYPE: Brain

(ix) FEATURE:

(A) NAME/KEY: sig\_peptide

(B) LOCATION: 45..86

(C) IDENTIFICATION METHOD: Von Heijne matrix

(D) OTHER INFORMATION: score 10.8

seq LLLLGLCLGLSLC/VG

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 38:

AGTGTCCCGC CGGGTCCCCG AGCGTCCCGC GCCCTCGCCC CGCC ATG CTC CTG CTG Met Leu Leu Leu CTG GGG CTG TGC CTG TGT GTG GGG TCG CAG GAA GAG 104

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	29	PCT/IB98/01236

WO 99/06552	29 P	CT/IB98/01:
<u> </u>	eu Ser Lau Cys Val Gly Ser Gln Glu Glu 1 5	
GCG CAG AGC TGG GGC CAC T Ala Gln Ser Trp Gly His S 10	CT TCG GAG CAG GAT GGA CTC AGG GTC CCG er Ser Glu Gln Asp Gly Leu Arg Val Pro 15 20	152
AGG Arg		155
(2) INFORMATION FOR SEQ I	D NO: 39:	
(i) SEQUENCE CHARAC' (A) LENGTH: 42 (B) TYPE: NUCI (C) STRANDEDNE (D) TOPOLOGY:	77 base pairs EIC ACID CSS: DOUBLE	·
(ii) MOLECULE TYPE:	CDNA	
(vi) ORIGINAL SOURCE (A) ORGANISM: (F) TISSUE TYP	Homo Sapiens	
(ix) FEATURE: (A) NAME/KEY: (B) LOCATION: (C) IDENTIFICA (D) OTHER INFO	191268 TION METHOD: Von Heijne matric	
(xi) SEQUENCE DESCRI	PTION: SEQ ID NO: 39:	
	ACAGAA AGWWCAATCC TTTAAGGGAG AACCTAGAAG	
	AGGCTT CCGAGGATTT GGTAGACAGA TCAGAGGCAC	
GTTTCCCACA ACTGCGAAGA GGCG	CTGAGG CAATTCTGCA AGAAGATTTT GGGGTTTTGG	180
AAAAGAAGCT ATG GAA AAC GGA Met Glu Asn Gly -25	GGG GCA GGC ACT CTG CAG ATA AGG CAA Gly Ala Gly Thr Leu Gln Ile Arg Gln -20 -15	229
GTC CTG CTT TTC TTT GTT TTC Val Leu Leu Phe Phe Val Leu -10	G CTG GGA ATG TCT CAG GCG GGC TCT GAA 1 Leu Gly Met Ser Gln Ala Gly Ser Glu -5	277
ACT GGG AAC TIT TIG GTG ATC Thr Gly Asn Phe Leu Val Met 5	G GAG GAA TTG CAG AGC GGG AGC TTT GTA Glu Glu Leu Gln Ser Gly Ser Phe Val 15	325
GGA AAT TTG GCA AAG ACC CTG Gly Asn Leu Ala Lys Thr Leu 20 25	G GGA CTC GAG GTG AGT GAG CTG TCT TCG I Gly Leu Glu Val Ser Glu Leu Ser Ser 30	373
CGG GGG GCT CGG GTG GTT TCG Arg Gly Ala Arg Val Val Ser 40	AAT GAT AAC AAA GAG TGT TTG CAG CTG Asn Asp Asn Lys Glu Cys Leu Gln Leu 45 50	421

GAC	ACG					427
Asp	Thr					

# (2) INFORMATION FOR SEQ ID NO: 40:

- (i) SEQUENCE CHARACTERISTICS:
  - (A) LENGTH: 398 base pairs
  - (B) TYPE: NUCLEIC ACID
  - (C) STRANDEDNESS: DOUBLE
  - (D) TOPOLOGY: LINEAR
- (ii) MOLECULE TYPE: CDNA
- (vi) ORIGINAL SOURCE:
  - (A) ORGANISM: Homo Sapiens
  - (F) TISSUE TYPE: Brain
- (ix) FEATURE:

-15

- (A) NAME/KEY: sig\_peptide
- (B) LOCATION: 12..389
- (C) IDENTIFICATION METHOD: Von Heijne matrix
- (D) OTHER INFORMATION: score 10

seq LKLLLFLSTELQA/SQ

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 40:

AAAAAAGGAC C ATG AGA GGG CCG GAG CCG GGT CCC CAA CCG ACG ATG GAG Met Arg Gly Pro Glu Pro Gly Pro Gln Pro Thr Met Glu -125 -120 -115	.50
GGA GAC GTG CTG GAC ACA CTG GAG GCG CTG GGG TAT AAA GGA CCA TTG Gly Asp Val Leu Asp Thr Leu Glu Ala Leu Gly Tyr Lys Gly Pro Leu -110 -105 -100	98
TTA GAA GAG CAA GCC CTT ACA AAG GCG GCA GAG GGT GGA TTA TCT TCA Leu Glu Glu Gln Ala Leu Thr Lys Ala Ala Glu Gly Gly Leu Ser Ser -95 -90 -85	146
CCT GAA TTT TCA GAG CTC TGT ATT TGG TTA GGC TCT CAA ATA AAA TCA Pro Glu Phe Ser Glu Leu Cys Ile Trp Leu Gly Ser Gln Ile Lys Ser -80 -75 -70	194
TTA TGC AAC TTG GAA GAA AGT ATC ACG TCT GCT GGA AGA GAT GAT CTA Leu Cys Asn Leu Glu Glu Ser Ile Thr Ser Ala Gly Arg Asp Asp Leu -65 -55 -50	242
GAG AGC TTC CAG CTT GAG ATA AGT GGC TTT TTA AAA GAA ATG GCA TGT Glu Ser Phe Gln Leu Glu Ile Ser Gly Phe Leu Lys Glu Met Ala Cys -45 -40 -35	290
CCA TAT TCT GTA CTC ATA TCA GGA GAT ATT AAA GAT CGT TTA AAA AAG Pro Tyr Ser Val Leu Ile Ser Gly Asp Ile Lys Asp Arg Leu Lys Lys -30 -25 -20	338
AAG GAG GAC TGT TTG AAA CTT CTA TTA TTT TTA AGT ACA GAA CTT CAA	386

Lys Glu Asp Cys Leu Lys Leu Leu Leu Phe Leu Ser Thr Glu Leu Gln

-10

VO 99/06552	31	PCT/IB98/01236
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GCT TCA CAG ATA Ala Ser Gln Ile 1	398
(2) INFORMATION FOR SEQ ID NO: 41:	
(i) SEQUENCE CHARACTERISTICS:  (A) LENGTH: 201 base pairs  (B) TYPE: NUCLEIC ACID  (C) STRANDEDNESS: DOUBLE  (D) TOPOLOGY: LINEAR	
(ii) MOLECULE TYPE: CDNA	
<pre>(vi) ORIGINAL SOURCE:     (A) ORGANISM: Homo Sapiens     (F) TISSUE TYPE: Brain</pre>	
<ul> <li>(ix) FEATURE:</li> <li>(A) NAME/KEY: sig_peptide</li> <li>(B) LOCATION: 70147</li> <li>(C) IDENTIFICATION METHOD: Von Heijne matrix</li> <li>(D) OTHER INFORMATION: score 9.6</li> <li>seq WLIALASWSWALC/RI</li> </ul>	
(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 41:	
ACCCCCTTT CCTCCCCCC CCCCACTCCC CACCTCTCCC CACCTCTCCC	
AGCCCGGTTT CGTGCCCGCG GCCGACTGCG CASCTGTCCG CGAGTCTGAG ATACTTACAG	60
AGAGCTACA ATG GAA AAG TCC TGG ATG CTG TGG AAC TTT GTT GAA AGA TGG Met Glu Lys Ser Trp Met Leu Trp Asn Phe Val Glu Arg Trp -25 -20 -15	111
CTA ATA GCC TTG GCT TCA TGG TCT TGG GCT CTC TGC CGT ATT TCT CTT Leu Ile Ala Leu Ala Ser Trp Ser Trp Ala Leu Cys Arg Ile Ser Leu -10 -5 1	159
TTA CCT TTA ATA GTG ACT TTT CAT CTG TAT GGA GGT TCG GGG Leu Pro Leu Ile Val Thr Phe His Leu Tyr Gly Gly Ser Gly 5 10 15	201
(2) INFORMATION FOR SEQ ID NO: 42:	
(i) SEQUENCE CHARACTERISTICS:  (A) LENGTH: 272 base pairs  (B) TYPE: NUCLEIC ACID  (C) STRANDEDNESS: DOUBLE  (D) TOPOLOGY: LINEAR	
(ii) MOLECULE TYPE: CDNA	
<pre>(vi) CPIGINAL SOURCE:    (A - ORGANISM: Homo Sapiens    F. TISSUE TYPE: Brain</pre>	

		.x) E	(A) (B) (C) (D)	NAME LOCA I DEN OTHE	C/KEY ATION ATIFI CR IN	: 6. CATI	.113 ON M	ETHO N:	D: V scor seq	e 9. LGLI	5 LLAP	e ma				
AGAT	T AT	rg c <i>i</i>	AG C# Ln G]	AG AG		SC AC	CA GA	AG GO	CT G1	rc Go	cg go	Ly Al			CT CAC	50
TGC Cys	CTG Leu -20	GGC Gly	TTC Phe	TGT Cys	GGA Gly	ATG Met -15	AGA Arg	CTC Leu	GGG Gly	CTC Leu	CTT Leu -10	CTA Leu	CTT Leu	GCA Ala	AGA Arg	98
														GAC Asp 10		146
														ACC Thr		194
CAG Gln	ACC Thr	TAC Tyr 30	AAC Asn	GGC Gly	CAG Gln	AGC Ser	GAG Glu 35	AAC Asn	AAC Asn	GAA Glu	GAC Asp	TAT Tyr 40	GAG Glu	ATC Ile	CCC Pro	242
					AAC Asn											272
(2)	INF	ORMA'	TION	FOR	SEQ	ID	NO:	43:								
(i) SEQUENCE CHARACTERISTICS:  (A) LENGTH: 186 base pairs  (B) TYPE: NUCLEIC ACID  (C) STRANDEDNESS: DOUBLE  (D) TOPOLOGY: LINEAR																

- (ii) MOLECULE TYPE: CDNA
- (vi) ORIGINAL SOURCE:
  - (A) ORGANISM: Homo Sapiens
  - (F) TISSUE TYPE: Brain
- (ix) FEATURE:
  - (A) NAME/KEY: sig\_peptide
  - (B) LOCATION: 28..99
  - (C) IDENTIFICATION METHOD: Von Heijne matrix
  - (D) OTHER INFORMATION: score 9.1

seq LVVFLLLPLASGP/QV

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 43:

33 Glu PCT/1B98/01236 WO 99/06552

		Met Glu Ly	rs Gly Asn Al -20	a Phe Leu Lys	
	GPT GTT TTT CTT Val Val Phe Leu -10				102
	AAA AGC GAA ATT Lys Ser Glu Ile 5				150
	TTC AAT AAA TTT Phe Asn Lys Phe				186
(ii) SE  (ii) M  (vi) O  (ix) E	QUENCE CHARACTEI (A) LENGTH: 400 (B) TYPE: NUCLE: (C) STRANDEDNES: (D) TOPOLOGY: L' OLECULE TYPE: C RIGINAL SOURCE: (A) ORGANISM: H (F) TISSUE TYPE  EATURE: (A) NAME/KEY: S (B) LOCATION: 1 (C) IDENTIFICAT (D) OTHER INFOR	RISTICS: base pairs IC ACID S: DOUBLE INEAR  DNA  omo Sapiens : Brain  ig_peptide 64235 ION METHOD: MATION: sco	re 9 LLMLIVFHAASN		
AGTTAATTTG A	ACAAAATAT AGTAA	GTATA CTATTA	TTTT CCATGTC	TTT CTAGGCTTTT	60
TAAACTCTGC 2	AGTGTATTTA CTGTA	ACTCTC GTAGAA	GGAG TGCCATC	AAC TGCAATTGGT	120
ACAAATTGTG (	CTTATTTTC TGCTC	CTTTTC ACGTTC		TTC CCA TTC Phe Pro Phe	175
	GGT CTT CCT ACT Gly Leu Pro The				223
	OCT TTA CAG AGA				27
	ICA GGA CTG ATC			Gln Ile Pro	311

CAT GAR ARE DEFACT CAT AND TOT GTC AND CAT GOT COO CTC AGT TOT 367

WO 99/06552 PCT/IB98/01236

34 His Glu Lys Leu Thr His Ile Ser Val Met His Gly Pro Leu Ser Ser 30 35 CAT CAC TCA TAC ACT CAC ATA CAT TTA TTT TTA 400 His His Ser Tyr Thr His Ile His Leu Phe Leu 50 (2) INFORMATION FOR SEQ ID NO: 45: (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 297 base pairs (B) TYPE: NUCLEIC ACID (C) STRANDEDNESS: DOUBLE (D) TOPOLOGY: LINEAR (ii) MOLECULE TYPE: CDNA (vi) ORIGINAL SOURCE: (A) ORGANISM: Homo Sapiens (F) TISSUE TYPE: Brain (ix) FEATURE: (A) NAME/KEY: sig\_peptide (B) LOCATION: 1..228 (C) IDENTIFICATION METHOD: Von Heijne matrix (D) OTHER INFORMATION: score 8.8 seq SLLLWMSSLPSLG/EK (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 45: ATG ACT TCA CGT AGC TTG CGT CGC TGC TCC TGT CTC CGT GTA ACT CAC 48 Met Thr Ser Arg Ser Leu Arg Arg Cys Ser Cys Leu Arg Val Thr His AAT AAA GAG ATT TTG GCA TCA ACC GTG AGC TTA GGG GTA GAA GGG TAT Asn Lys Glu Ile Leu Ala Ser Thr Val Ser Leu Gly Val Glu Gly Tyr ATG TTA GGA GGT GGG AGC AGA ATC AAT TCT TCA AAT CTT AAT GAT GGT 144 Met Leu Gly Gly Ser Arg Ile Asn Ser Ser Asn Leu Asn Asp Gly GAA GAA GAG TGC TCA CCA GAT TCC CTT CTG GTC TGG AAA AAG AAA TCC 192 Glu Glu Glu Cys Ser Pro Asp Ser Leu Leu Val Trp Lys Lys Ser -25-20 CTT CTT TTG TGG ATG TCA TCT CTA CCA TCT CTC GGT GAA AAA TAT TTC Leu Leu Trp Met Ser Ser Leu Pro Ser Leu Gly Glu Lys Tyr Phe AAG AGA ATO CTA AGA TGG AGA GAG CAT TGG AAG TCA TCC GGC CCA ATT 288 Lys Arg Ile Leu Arg Trp Arg Glu His Trp Lys Ser Ser Gly Pro Ile 10 15

297

CCC TTG TGG

Pro Leu Trp

(2	) 11/1	FORT	ATIO	N FO	R SE	Q ID	NO:	46:								
		(1)	(A) (B) (C)	) LEI ) TYI ) STI	CHAI NGTH: PE: N RANDE	: 21. NUCL: EDNES	3 ba: EIC A SS: [	se pa ACID DOUBI	airs							
		(ii)	MOLE	ECUL	E TYE	PE: (	CDNA									
	,	(vi)	(A)	ORG	SOU SANIS	M: F	omo	Sapi ain	ens							
			(B) (C) (D)	NAM LOC IDE OTH	E/KE ATIO NTIF ER I	N: 1 ICAT NFOR	01 ION MATI	68 METH ON:	OD: sco seq	re 8 ILL	.8 LLTV					·
	(	21.)	SEQU	ENCE	DES	CRIP	TION	: SE	Q ID	NO:	46:					
				-	-	50		ra 11	ec A	sp P	ne A 45	rg T	hr C	ys I	TT GCC le Ala ~40	51
				-35	TTG Leu	Cys	Tyl	Val	~30	Ala	Cys	Arg	Ala	Leu -25	Met	99
			-20		CTG Leu	Gry	Leu	-15	Ala	He	Leu	Leu	Leu -10	Leu	Thr	147
STT /al	CTT Leu	CCC Pro -5	TGC Cys	ATC Ile	SGG Xaa	ATG Met	GGC Gly l	CAG Gln	GAG Glu	CCC Pro	GGT Gly 5	GTG Val	GCT Ala	AAG Lys	TAC Tyr	195
AGG Arg 10	SGG Xaa	GCC Ala	CAG Gln	CTG Leu	GCT Ala 15											213
2)	INFO	PAHA	NOI	FOR	SEQ	ID N	10: 4	7:								
	(1	) 32	(A) (B) (C)	LENG TYPE STRA	HARA TH: : NU NDED LOGY	319 CLEI NESS	base C AC : DO	pai ID UBLE								
	: -	i H	DLEC	ULE	TYPE	: CD	NA									
	(V		(A)	ORGA	SOUR NISM UE T	: Но	mo S. Bra.	apie: in	ns							

<pre>(ix) FEATURE:     (A) NAME/KEY: sig_peptide     (B) LOCATION: 62196     (C) IDENTIFICATION METHOD: Von Heijne matrix     (D) OTHER INFORMATION: score 8.5</pre>									
(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 47:									
ATTGGTGCAG AGGCCCTTCT TGTCTCCACA CCAGAAGGAG CTGAGCAGAG GGGCCACAGC	60								
G ATG GGA CCC CCT CCA ACC CAC ATT AAA TAC CTC CAC CTG AAT ATT TAT Met Gly Pro Pro Pro Thr His Ile Lys Tyr Leu His Leu Asn Ile Tyr -45 -35 -30									
TGC AAC GGC AAG AGC ACT GCA CCT GGA ATC CGG TCT CAC AGC CTT GGA Cys Asn Gly Lys Ser Thr Ala Pro Gly Ile Arg Ser His Ser Leu Gly -25 -15	157								
TTT GCC TTG CTA AGC CTC AGT CAT CCA ACC TGC CAG GCA GGT GCA CCT Phe Ala Leu Leu Ser Leu Ser His Pro Thr Cys Gln Ala Gly Ala Pro -10 -5 1	205								
GCC GCA GCC CTG CCT TCT CTG TGG AGC TGG TGC TCT CGG GGT GCA CGA Ala Ala Ala Leu Pro Ser Leu Trp Ser Trp Cys Ser Arg Gly Ala Arg 5 10 15	253								
GTC AGG GTT GGG AGG ATG CTT TCT CAC CTG TAC ACC TGT GGA TGG TAC Val Arg Val Gly Arg Met Leu Ser His Leu Tyr Thr Cys Gly Trp Tyr 20 25 30 35	301								
GAT CAC AAC CCC CAT GGG Asp His Asn Pro His Gly 40	319								
(2) INFORMATION FOR SEQ ID NO: 48:									
(i) SEQUENCE CHARACTERISTICS:  (A) LENGTH: 260 base pairs  (B) TYPE: NUCLEIC ACID  (C) STRANDEDNESS: DOUBLE  (D) TOPOLOGY: LINEAR									
(ii) MOLECULE TYPE: CDNA									
<ul><li>(vi) ORIGINAL SOURCE:</li><li>(A) ORGANISM: Homo Sapiens</li><li>(F) TISSUE TYPE: Brain</li></ul>									
<pre>(ix) FEATURE:     (A) NAME/KEY: sig_peptide     (B) LOCATION: 204251     (C) IDENTIFICATION METHOD: Von Heijne matrix     (D) OTHER INFORMATION: score 8.5</pre>									

(MI) SEQUENCE DESCRIPTION: SEQ ID NO: 48:

seq LLTFLAFTTLLFA/PP

ACTGTTATTC TTUACATATT ATCTCTATTA GTADVWGGCT TCTAGTCACC CAAGTTAGAA	60
ATCTGTGAGT CATCTTTGT TTCTTCCCTT TCCCTTACTG TTTAGTTTTA ATTGCTAAGT	120
CTTGTTANTA CTACATCAGG TATGATTTTA AAAACATTTT TGATGTTCTA CTGCCACCAC	180
CTTAGTTCTG GTACTCATTT TGC ATG TTT TGT CTT TTG ACT TTC CTT GCT TTT  Met Phe Cys Leu Leu Thr Phe Leu Ala Phe  -15 -10	233
ACA ACT CTT CTT TTC GCA CCC CCA TGG Thr Thr Leu Leu Phe Ala Pro Pro Trp -5	260
(2) INFORMATION FOR SEQ ID NO: 49:	
<ul><li>(i) SEQUENCE CHARACTERISTICS:</li><li>(A) LENGTH: 365 base pairs</li><li>(B) TYPE: NUCLEIC ACID</li><li>(C) STRANDEDNESS: DOUBLE</li><li>(D) TOPOLOGY: LINEAR</li></ul>	
(ii) MOLECULE TYPE: CDNA	
<pre>(vi) ORIGINAL SOURCE:    (A) ORGANISM: Homo Sapiens    (F) TISSUE TYPE: Brain</pre>	
<ul> <li>(ix) FEATURE:</li> <li>(A) NAME/KEY: sig_peptide</li> <li>(B) LOCATION: 126212</li> <li>(C) IDENTIFICATION METHOD: Von Heijne matrix</li> <li>(D) OTHER INFORMATION: score 8.4</li> <li>seq LKCLLAVLSSLFA/AI</li> </ul>	
(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 49:	
ACABATGTGT TATGATTTTC CAGGCCCTTC TTCATCTGCT CTCCCTTCCT TTTGAGCATT	60
ATCCCATTTC ATGCCCCCAC ACAGATTCTA GCCATACCCC ATGACTTACA ATTTCCCCAC	120
AAAGA ATG CAC TGT GGC TCC ACT CCA GGA CTT TGC CCA TGC TGG GTC CCC Met His Cys Gly Ser Thr Pro Gly Leu Cys Pro Cys Trp Val Pro -25 -20 -15	170
TTC CTG AAA TGC CTT CTA GCT GTT CTC TCT TCC CTG TTT GCT GCC ATT Phe Led Lys Cys Leu Leu Ala Val Leu Sex Ser Leu Phe Ala Ala Ile -10 -5 1	218
TCC GTV GAC AGA CTA TAC TTG TCT TTC TGT TCT AAT TGC TCT GAA ATA Ser Val Aug Arg Leu Tyr Leu Ser Phe Cys Ser Asn Cys Ser Glu Ile 3 10 15	266
TAC CTUINGS CCC CCC AGC TTT CCT GCT CCC CCA TCC CCT GTA GTC CTT  Tyr Ly lrp Pro Pro Ser Phe Pro Ala Pro Pro Ser Pro Val Val Leu  25	314

WO 99/06552 38 CTA GTT TTC CTG TGT CCC CAT GGG ACT TCT TTA TCC TTT TTG AAG CTA 362 Leu Val Phe Leu Cys Pro His Gly Thr Ser Leu Ser Phe Leu Lys Leu 40 CCG 365 Pro (2) INFORMATION FOR SEQ ID NO: 50: (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 69 base pairs (B) TYPE: NUCLEIC ACID (C) STRANDEDNESS: DOUBLE (D) TOPOLOGY: LINEAR (ii) MOLECULE TYPE: CDNA (vi) ORIGINAL SOURCE: (A) ORGANISM: Homo Sapiens (F) TISSUE TYPE: Brain (ix) FEATURE: (A) NAME/KEY: sig\_peptide (B) LOCATION: 1..48 (C) IDENTIFICATION METHOD: Von Heijne matrix (D) OTHER INFORMATION: score 8.3 seq VCSALLLLGIVSS/KP (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 50: ATG AAT TTA GTT TGT TCA GCT CTT TTA CTT CTT GGA ATA GTA TCT TCC 48 Met Asn Leu Val Cys Ser Ala Leu Leu Leu Leu Gly Ile Val Ser Ser -15-10 AAA CCC TAT ATG AGA AAG CGG 69 Lys Pro Tyr Met Arg Lys Arg (2) INFORMATION FOR SEQ ID NO: 51: (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 184 base pairs (3) TYPE: NUCLEIC ACID (C) STRANDEDNESS: DOUBLE (D) TOPOLOGY: LINEAR (ii) MOLECULE TYPE: CDNA (vi) ORIGINAL SOURCE: (A) ORGANISM: Homo Sapiens (F) TISSUE TYPE: Brain

(ix) FEATURE:

(A) NAME/KEY: sig\_peptide (B) LOCATION: 44..148

(C) IDENTIFICATION METHOD: Von Heijne matrix

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		3,9		
(D) OTF	ER INFORMATION:	score 8.3 seq AAMLIGL	LAWLQT/VP	
(xi) SEQUENCE	DESCRIPTION: SEC	Q ID NO: 51:		
AAATTACAAG AAAGCTGG	AC TTGCCGCTGT GG1	ICTCAGGA GAA	ATG AGT GTT CTT Met Ser Val Leu -35	5
GAT GAC AGG CAA AGG Asp Asp Arg Gln Arg -30	-25	-20	Arg His Ser Ser	10
CTG GAA GCC GCC ATG Leu Glu Ala Ala Met -15	TTA ATA GGA TTA Leu Ile Gly Leu -10	CTA GCC TGG Leu Ala Trp -5	CTC CAG ACA GTG Leu Gln Thr Val	151
CCT GCT CAT GGC TGC Pro Ala His Gly Cys 5	CAG TTC TTA CCG Gln Phe Leu Pro 10	ATC CGG Ile Arg		184
(A) LENG (B) TYPE (C) STRA (D) TOPO  (ii) MOLECULE  (vi) ORIGINAL (A) ORGA (F) TISS  (ix) FEATURE: (A) NAME (B) LOCA (C) IDEN (D) OTHE	CHARACTERISTICS: TH: 251 base pair :: NUCLEIC ACID .NDEDNESS: DOUBLE .NDEDNESS: DOUB	ns : Von Heijne Core 8.3 eq LLIICHYLE		
ACTITITIT CACTITCCT. COTGAAGCA ATAGCTAGT.	A CTTTCCCTCC TTCC	GCCCAT GATGO	CCAATG ACTAGCTCTG	60
PATCAATAC CAGTAAA A	TG GGT GTC AAG GG	IGCCAC CTAGO	ATCCA GCCGAACCTT	120
-: -:	20	y Arg Arg Le -15	eu Leu Ile Ile -10	170
GC TAT TAT TTA CCT ( VA His Tyr Leu Pro : -5	CTG AGT CTG TGC A Leu Ser Leu Cys I	TT CCC ATT C le Pro Ile F 1	CT TCC CAT ATT ro Ser His Ile 5	213

251

ACC THE STO COG CGC AAC ACC CCC CCT GTC AGG

Asn	Ser	Leu	Pro	Arg	Asn	Thr	Pro	Pro	Val	Arg
		10					15			_

(2)	INFORMATION	FOR	SEO	ΤD	NO:	53:

- (i) SEQUENCE CHARACTERISTICS:
  - (A) LENGTH: 154 base pairs
  - (B) TYPE: NUCLEIC ACID
  - (C) STRANDEDNESS: DOUBLE
  - (D) TOPOLOGY: LINEAR
- (ii) MOLECULE TYPE: CDNA
- (vi) ORIGINAL SOURCE:
  - (A) ORGANISM: Homo Sapiens
  - (F) TISSUE TYPE: Brain
- (ix) FEATURE:
  - (A) NAME/KEY: sig\_peptide
  - (B) LOCATION: 26..118
  - (C) IDENTIFICATION METHOD: Von Heijne matrix
  - (D) OTHER INFORMATION: score 8.2

seq LECLLLYLAESSG/LR

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 53:

ACAGAACTAA CCTAGAAAGA ATGAT ATG AAA CTT CGT GAG TGC CCG GCC CTC

Met Lys Leu Arg Glu Cys Pro Ala Leu

-30

-25

CGA TGG TCC CAG CTG TCC CAG CAC AAG CTG GAG TGT CTA TTG CTT TAC

Arg Trp Ser Gln Leu Ser Gln His Lys Leu Glu Cys Leu Leu Leu Tyr

-20

-15

-10

CTG GCA GAG AGC TCC GGG CTC AGA ACA GGA AAT GTG GGA GTT CTC CAC
Leu Ala Glu Ser Ser Gly Leu Arg Thr Gly Asn Val Gly Val Leu His
-5 1 5 10

CCA AGG
Pro Arg

## (2) INFORMATION FOR SEQ ID NO: 54:

- (i) SEQUENCE CHARACTERISTICS:
  - (A) LENGTH: 485 base pairs
  - (B) TYPE: NUCLEIC ACID
  - (C) STRANDEDNESS: DOUBLE
  - (D) TOPOLOGY: LINEAR
- (ii) MOLECULE TYPE: CDNA
- (vi) ORIGINAL SOURCE:
  - (A) ORGANISM: Homo Sapiens
  - (F) TISSUE TYPE: Brain
- (ix) FEATURE:

			(B) (C)	LOCA IDEN	TION TIFI	: si I: 78 CATI IFORM	40 ON M	4 ETHO	D: V	e 8.	2		trix BA/GE			
	( >	i) S	EQUE	NCE	DESC	RIPI	:NOI	SEÇ	) ID	NO:	54:					
ACCC	TTTC	GT C	CCGCI	CTCF	AT TO	GCTC	CTGCT	GC <i>E</i>	AGCCC	CTGA	CCAF	CGC1	CC F	ATAC	SGCCGG	60
GATO	CAGO	CA T	TACTI			SAT ( Asp E		Arg (					Ala E			110
AAG Lys	CGG Arg	CAG Gln	AAA Lys -95	ATT Ile	CAT His	GCT Ala	GAT Asp	GCA Ala -90	TCA Ser	TCA Ser	AAA Lys	GTA Val	CTT Leu -85	GCA Ala	AAG Lys	158
						GGA Gly										206
						CGC Arg -60										254
						GTT Val										302
						CAC His										350
						CTC Leu										398
						CTG Leu 5										446
GCT Ala 15	GGT Gly	GGA Gly	TGT Cys	AGC Ser	TGG Trp 20	ATT Ile	CAG Gln	CAT His	CTT Leu	CAT His 25	CCC Pro	AGT Ser				485
.?.;	INF	ORMA	TION	FOR	SEQ	ΙD	NO:	55:								
	(	i) S	(A) (B) (C)	LENO TYP: STR	GTH: E: N ANDE	ACTE 276 UCLE DNES Y: L	base IC AG S: DG	e pa CID OUBL								

(ii) MOLECULE TYPE: CDNA
(vi) ORIGINAL SOURCE:

(A) ORGANISM: Homo Sapiens

(E)	TISSUE	TYPE:	Brain

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١	1	×	}	7 7		. 1	U.	к	Ŀ	:

- (A) NAME/KEY: sig\_peptide
- (B) LOCATION: 199..261
- (C) IDENTIFICATION METHOD: Von Heijne matrix
- (D) OTHER INFORMATION: score 8

seq LFLVAVLVKVAEA/RK

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 55:

AGCCTCTCCT GCACCCTCAG CCGGCGCGCT TCTCTTATGG GCGTCTGCTG CAGTCTGGCT 60 GCGGTCGAAC TGAAAGCGGC GGCGGGAGAC CAAACTTAGA CCCCGCTGTG GACTAGAGAA 120 CTCAGAGAAG GCAGAGGGAG AGGGAGAGAG AGASABWBAA GGGACCCGAG GAGGAGGCTT 180 CCATCACGTC ATTGCAGG ATG TTC TGG AAG CTT TCC CTG TCC TTG TTC CTG 231 Met Phe Trp Lys Leu Ser Leu Ser Leu Phe Leu GTG GCG GTG CTG GTG AAG GTG GCG GAA GCC CGG AAG AAC CGG TCG 276 Val Ala Val Leu Val Lys Val Ala Glu Ala Arg Lys Asn Arg Ser -5

#### (2) INFORMATION FOR SEQ ID NO: 56:

- (i) SEQUENCE CHARACTERISTICS:
  - (A) LENGTH: 197 base pairs

  - (B) TYPE: NUCLEIC ACID
    (C) STRANDEDNESS: DOUBLE
  - (D) TOPOLOGY: LINEAR
- (ii) MOLECULE TYPE: CDNA
- (vi) ORIGINAL SOURCE:
  - (A) ORGANISM: Homo Sapiens
  - (F) TISSUE TYPE: Brain
- (ix) FEATURE:
  - (A) NAME/KEY: sig\_peptide
  - (B) LOCATION: 120..173
  - (C) IDENTIFICATION METHOD: Von Heijne matrix
  - (D) OTHER INFORMATION: score 7.9

seq LFSLLVLQSMATG/AT

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 56:

AAGTTTCCCG GGAGAGACGA AAGCAGGAAC GAGAGCGGAG GNAGCACAGT CCGCCGAGCA	60
CAAGCTCCAG CATCCCGTCA GGGGTTGCAG GTGTGTGGGA GGCTTGAAAC TGTTACAAT	119
ATG GOT TTC CTT GGA CTC TTC TCT TTG CTG GTT CTG CAA AGT ATG GCT Met Ala Phe Leu Gly Leu Phe Ser Leu Leu Val Leu Gln Ser Met Ala -15 -5	167
AGA GGG GCC ACT TTC CCT GAG GAA GCC CCG	197

Thr Gly Ala Thr Phe Pro Glu Glu Ala Pro

(2	) 10	FORM	ATIO	N FO	R SE	) IN	NO.	6.7								
			SEQUI (A) (B) (C)	ENCE LEN TYI	CHAINGTH: PE: NRANDE	RACTI 299 NUCLE	ERIS' Das EIC # SS: [	TICS se pa ACID	airs							
	(	(ii)	MOLE	CCULE	E TYE	PE: (	DNA									
	(	(vi)	(A)	ORG	SOU SANIS	М: Н	omo	Sapi ain	ens							•
	(	i×)	(C)	NAM LOC I DE	E/KE ATIO NTIF ER I	N: 9 ICAT	01 ION	43 METH	OD: sco	re 7	. 9		atrí TG/A			
	.(	xi)	SEQU	ENCE	DES	CRIP	MOIT	: SE								
	GAGC	GCD														
															TTGCAG	60
GTG	TGTG							ATG	GCT	TTC	CTT	GGA	CTC		<b>T</b> CT	60 113
TTG		GGA GTT	GGCT CTG	TGAA CAA	AC T	GTTA	CAAT	ATG Met	GCT Ala	TTC Phe	CTT Leu -15	GGA Gly	CTC Leu	TTC Phe	TCT Ser	
TTG Leu -10 GCC	TGTG CTG	GGA GTT Val GCT	GGCT CTG Leu GAC	TGAA CAA Gln TTG	AGT Ser -5	ATG Met	CAAT GCT Ala	ATG Met ACA Thr	GCT Ala GGG Gly	TTC Phe GCC Ala	CTT Leu -15 ACT Thr	GGA Gly TTC Phe	CTC Leu CCT Pro	TTC Phe GAG Glu 5	TCT Ser GAA Glu	113
TTG Leu -10 GCC Ala GGA Gly	CTG Leu ATT Ile AGC Ser	GGA GTT Val GCT Ala TGG Trp 25	CTG Leu GAC Asp 10 AGA Arg	CAA Gln TTG Leu AGG Arg	AGT Ser -5 TCA Ser GAA Glu	ATG Met GTG Val GGA Gly	GCT Ala AAT Asn GCC Ala 30	ATG Met ACA Thr ATG Met 15 AGC Ser	GCT Ala GGG Gly TAT Tyr AGA Arg	TTC Phe GCC Ala 1 AAT ASD	CTT Leu -15 ACT Thr CGT Arg	GGA Gly TTC Phe CTT Leu GCT Ala 35	CTC Leu CCT Pro AGA Arg 20 TCG Ser	TTC Phe GAG Glu 5 GCA Ala	TCT Ser GAA Glu GTT Val	113
TTG Leu -10 GCC Ala GGA Gly	TGTG CTG Leu ATT Ile	GGA GTT Val GCT Ala TGG Trp 25	CTG Leu GAC Asp 10 AGA Arg	CAA Gln TTG Leu AGG Arg	AGT Ser -5 TCA Ser GAA Glu	ATG Met GTG Val GGA Gly	GCT Ala  AAT Asn  GCC Ala 30	ATG Met ACA Thr ATG Met 15 AGC Ser	GCT Ala GGG Gly TAT Tyr AGA Arg	TTC Phe GCC Ala 1 AAT ASN CAA Gln	CTT Leu -15 ACT Thr CGT Arg	GGA Gly TTC Phe CTT Leu GCT Ala 35	CTC Leu CCT Pro AGA Arg 20 TCG Ser	TTC Phe GAG Glu 5 GCA Ala	TCT Ser GAA Glu GTT Val	113 161 209

(2) INFORMATION FOR SEQ ID NO: 58:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 370 base pairs
(B) TYPE: NUCLEIC ACID
(C) STRANDEDNESS: DOUBLE
(D) TOPOLOGY: LINEAR

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	(i	i) M	OLEC	ULE	TYPE	: CD	NA									
	( v	i) č	RIGI (A) (F)	ORGA	NISM	: Ho			ns							
	(i	×) E	(C)	name Loca	TION TIFI	: 62 CATI	22 ON M	6 Etho N:	D: V scor	e 7.	eijn 8 ALLF					
	(x	i) S	EQUE	NCE	DESC	RIPT	'ION:	SEC	ID	NO:	58:					•
AAGT	'GAGA	AA (	GAGC	TTAC	C AP	AGGC	CAGTO	TAC	GAAG	SAAG	GTTC	CTGC	GA C	SACTG	TCAGA	60
	t Se					n Ph					.a As				C TCT r Ser -40	109
														GGA Gly -25		157
														GCT Ala		205
														ATG Met		253
														CCC Pro		301
														ACG Thr 40		349
			GAG Glu 45													370
(2)	INF	ORMA	NOIT	FOR	SEQ	ID	NO:	59:								
	(	i) S	(B) (C)	NCE LEN TYP STR TOP	GTH: E: N ANDE	336 UCLE DNES	bas IC A S: D	e pa CID OUBL								
	(	ii)	MOLE	CULE	TYP	E: C	DNA									

(vi) ORIGINAL SOURCE:

(A) ORGANISM: Homo Sapiens
(F) TISSUE TYPE: Brain

	(i	ж) ! !	(B) (C)	NAME LOCA IDEN	TION TIFI	: si  : 91  CATI  FORM	33 ON M	O ETHC	D: V	on H	_	e ma	trix			
			(2)							LVLF		LLVT	P/TS			
	( ×	:i) :	SEQUE	NCE	DESC	RIPT	'ION:	SEC	) ID	NO:	59:					
rat:	CCTT	GG .	AGTTC	CAC	SA CT	GAAT	TAAC	G ACT	rgtto	STGG	GRDO	CATI	TA)	TTCA	\AATAC	60
rtg(	CCTA	ATA '	TTCGI	GTTC	SA GO	GTTC	CACAC		: Sei					ı Ala	CTT Leu	114
			TAT Tyr													162
			AGC Ser													210
			ACA Thr													258
			ATT										-			306
			CTG Leu -5													336
(2)	INF	ORMA	NOITA	FOR	SEQ	ID	NO:	60:								
	(	i) S	(B) (C)	LENG TYPI STR	GTH: E: N ANDE	ACTE: 394 UCLE DNES: Y: L	bas IC A S: D	e pa CID OUBL								
	(	ii)	MOLE	CULE	TYP	E: C	DNA									
	(	vi)		ORG	ANIS	RCE: M: H TYPE		-	ens							
	(	ix)		NAM	E/KE	Y: s N: 2			de							

(C) IDENTIFICATION METHOD: Von Heijne matrix
(D) OTHER INFORMATION: score 7.7
seq LQLLCCIFTLVLQ/HY

(MI) SEQUENCE DESCRIPTION: SEQ ID NO: 60:

ATACTA	PAA1.	GCTAC	SAATTO	AC'	TTGG	SAGTO	AAC	GCGA	GTT	CCAT	AGGT	TT A	AATGO	GTGGC	60
ACCTA:	CTCA	ACAAC	TGCA	AA'	TCAC	CTGTA	ACT	TGTA	LAAA	AATO	CCAG	GG (	CCACT	CATGG	120
ACAGC	CACAT	CTTTA	AACCO	AC	ACAP	TAAA	ACA	GACA	CTT	TGAT	TACA	TG A	AAAGT	TAGAA	180
GCTCTA	AAACT	AGAGO	CAAGGI	CAC	GTTC	STGGT	' AAC	SAAGO	TAT	TAGA	ATTCF	AG (	CATCO	ACAAA	240
AGTTT	ATAGT	CTGTC	CAGTC	A TA	AGG								CAG Gln		292
CTC TO Leu Cy -10															340
CAT CO															388
CAG C															394

## (2) INFORMATION FOR SEQ ID NO: 61:

- (i) SEQUENCE CHARACTERISTICS:
  - (A) LENGTH: 429 base pairs
  - (B) TYPE: NUCLEIC ACID
  - (C) STRANDEDNESS: DOUBLE
  - (D) TOPOLOGY: LINEAR
- (ii) MOLECULE TYPE: CDNA
- (vi) ORIGINAL SOURCE:
  - (A) ORGANISM: Homo Sapiens
  - (F) TISSUE TYPE: Brain
- (ix) FEATURE:
  - (A) NAME/KEY: sig\_peptide
  - (B) LOCATION: 208..264
  - (C) IDENTIFICATION METHOD: Von Heijne matrix
  - (D) OTHER INFORMATION: score 7.6

seq LLNLLLLSLFAGL/DP

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 61:

GAGAATGCCT GCNGAATGAT CGCCCCCCAG GGCGGCTGCC GCCGCTGCCG CTGCTGCTGT 60 TATTGCTACT GCTGCTGCCG CCGCCTCTGC TTCCACTCGG CTCTGACTGG, CAGGCARAAA 120 RTGCAACTTG AMSGARGGRH ARGTCTCTGG CAGTGAGTGG AGAGCCTACA TAAAAGAGAG 180 TAAAGAGGGG CAAAAACCCA GATCAGA ATG CAG GCG ACG TCC AAC CTT CTC AAC 234 Met Gln Ala Thr Ser Asn Leu Leu Asn

WO 99/06552		47		PCT/IB98/01236
CTC CTG CTG CTG TCT Leu Leu Leu Leu Ser -10	TTG TTT GOO G Leu Pho Ala G -5	GGA TTA GAT CCT T Bly Leu Asp Pro S 1	CC AAG AAC er Lys Asn 5	AAA 282 Lys
AAG AGA GGA AGT TCT Lys Arg Gly Ser Ser 10				
CCA TTC CTA NGA TCC Pro Pne Leu Xaa Ser 25				
TAT GGA CTA AAC ATG Tyr Gly Leu Asn Met 40				
TTG Leu 55				429
(2) INFORMATION FOR	. SEQ ID NO: 62	2:		
(A) LEN (B) TYP (C) STR	CHARACTERISTIC GTH: 189 base E: NUCLEIC ACI ANDEDNESS: DOU OLOGY: LINEAR	pairs ID		
(ii) MOLECULE	TYPE: CDNA			
	, SOURCE: ANISM: Homo Sa SUE TYPE: Brai	•		
(B) LOC (C) IDE	ME/KEY: sig_per MATION: 88180	) ETHOD: Von Heijne		
(xi) SEQUENCE	DESCRIPTION:	SEQ ID NO: 62:		
AACAGGCGTA ASKACATO	GGC CCAGCTCGAT	CCCTCCCTTT TGTT	CAACAA ACTA	AATTCG 60
AGCAGGAGGC TCTAGGA		G ATG AAA TGG AA t Met Lys Trp Ly -30	· · ·	
GGA TOG GTT COT TG Gly Ser Val Pro Cy -20				
OCA GOO TOO CAT TO	G TOT SOC CON	CCZ		199

189

CCA GGG TOG CAT TGG TGT GCC CCA CCA Pro Gly Ser His Trp Cys Ala Pro Pro

(2)	INFOR	MAT	ION	FOR	SEQ	ID N	10: 6	33:								
	(i)		(A) (B) (C)	LENG TYPE STRA	TH: : NU .NDED	CLEI	base C AC : DC	pai ID UBLE								
	(ii	) M	OLEC	ULE	TYPE	: CD	NA									
	(vi		(A)	ORGA				apie in	ns							
	(ix		(B) (C)	NAME LOCA IDEN	TION TIFI	: 10	66 ON M	ETHO	D: V	e 7.	6	e ma				
	(xi	) S	EQUE	NCE	DESC	RIPT	'ION :	SEC	) ID	NO:	63:					
AAGA	ATCAGA						er As				sn Le				G TCT u Ser	51
TTG Leu -5	TTT G	CC la	GGA Gly	TTA Leu	GAT Asp 1	CCT Pro	TCC Ser	AAG Lys	ACT Thr 5	CAG Gln	ATT Ile	AGT Ser	CCT Pro	AAA Lys 10	GAA Glu	99
GGG Gly	TGG C	CAG Sln	GTG Val 15	TAC Tyr	AGC Ser	TCA Ser	GCT Ala	CAG Gln 20	GAT Asp	CCT Pro	GAT Asp	GGG Gly	CGG Arg 25	TGC Cys	ATT Ile	147
TGC Cys	ACA C	GTT /al 30	GTW Val	GCT Ala	CCA Pro	GAA Glu	CAA Gln 35	AAC Asn	CTG Leu	TGT Cys	TCC Ser	CGG Arg 40	GAT Asp	GCC Ala	AAA Lys	195
	AGG ( Arg ( 45															243
(2)	INFO	RMA:	rion	FOR	SEQ	ID	NO:	64:								
	(i)	) Si	(A) (B) (C)	LENG TYP	GTH: E: N ANDE	UCLE	bas IC A S: D	e pa CID OUBL								
	(i:	i) i	MOLE	CULE	TYP	E: C	DNA									

(vi) ORIGINAL SOURCE:

(A) ORGANISM: Homo Sapiens (F) TISSUE TYPE: Brain

	(	(ix)	(B)	NAM LOC I DE	E/KE CATIC CNTIE	Y: s N: 1 ICAT NFOR	58 ION	301 METH	OD: sco	re 7	. 5		atri VS/L			
	(	xi)	SEQU	ENCE	DES	CRIP	TION	: SE	Q ID	NO:	64:					
ACA	AACA	GAC	GMTA	.CCAT	CG C	TTCA	GCAG	C AT	CCTC	TCAG	ACA	AGAG	CCA	CTAT	TTCTGA	60
															ACTGAA	120
CCA	AAAA	GAT	TCAA	AAGA	GC A	AGTG	GAAT	с тс	TAAG.	A AT	G GC t Al	T TC a Se	C AG r Se -4	r Hi	C TGG s Trp	175
	GAA Glu	-40	1112	1111	Set	Val	-35	Gin	Tyr	Leu	Gly	Phe -30	Gln	Val	Gln	223
AAA Lys	ATT Ile -25	TAC Tyr	CCT Pro	TTC Phe	CAT His	GAC Asp -20	AAC Asn	TGG Trp	AAC Asn	ACT Thr	GCC Ala -15	TGC Cys	TTT Phe	GTC Val	ATC Ile	271
CTG Leu -10	CTT Leu	TTA Leu	TTT Phe	ATA Ile	TTT Phe -5	ACA Thr	GTG Val	GTA Val	TCT Ser	TTA Leu 1	GTG Val	GTG Val	CTG Leu	GCT Ala 5	TTC Phe	319
CTT Leu	TAT Tyr	GAA Glu	GTG Val 10	CTT Leu	GAC Asp	TGC Cys	TGC Cys	TGC Cys 15	TGT Cys	GTA Val	AAA Lys	AAC Asn	AAA Lys 20	ACC Thr	GTG Val	367
AAA Lys	GAC Asp	TTG Leu 25	AAA Lys	AGT Ser	GAA Glu	CCC Pro	AAC Asn 30	CCT Pro	CGG Arg							397
(2)		) SE	QUEN (A) (B) (C)	CE C LENG TYPE STRA	HARA TH: : NU NDED	ID N CTER 182 CLEI NESS : LI	ISTI base C AC : DO	CS: pai ID UBLE	rs							
	( )	1) M	OLEC	ULE	TYFE	: CD	NA									

(vi) ORIGINAL SOURCE:

(ix) FEATURE:

(A) ORGANICM: Homo Sapiens
(F) TISSUE TYPE: Brain

(A) NAME/KEY: sig\_peptide
(B) LOCATION: 78..176
(C) IDENTIFICATION METHOD: Von Heijne matrix
(D) OTHER INFORMATION: score 7.4

sed ITCCVLLLLNCSG/VW

(xi)	SEQUENCE	DESCRIPTION:	SEO	ID N	0:	65:

ATCGACTGTG AGCTGCGGCA GAGAGCAGAG GCGGCGGCGC GGGACCTGCA GTCGCCAGGG 60 ATTCCCTCCA GGTGACG ATG CTC TGG TTC TCC GGC GTC GGG GCT CTG GCT 110 Met Leu Trp Phe Ser Gly Val Gly Ala Leu Ala GAG CGT TAC TGC CGC CGC TCG CCT GGG ATT ACG TGC TGC GTC TTG CTG Glu Arg Tyr Cys Arg Arg Ser Pro Gly Ile Thr Cys Cys Val Leu Leu -20 CTA CTC AAT TGC TCA GGG GTC TGG 182 Leu Leu Asn Cys Ser Gly Val Trp (2) INFORMATION FOR SEQ ID NO: 66: (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 256 base pairs (B) TYPE: NUCLEIC ACID (C) STRANDEDNESS: DOUBLE (D) TOPOLOGY: LINEAR (ii) MOLECULE TYPE: CDNA (vi) ORIGINAL SOURCE: (A) ORGANISM: Homo Sapiens (F) TISSUE TYPE: Brain (ix) FEATURE: (A) NAME/KEY: sig\_peptide (B) LOCATION: 164..238 (C) IDENTIFICATION METHOD: Von Heijne matrix (D) OTHER INFORMATION: score 7.3 seq LIFFLNVTQLVRG/RG (xi) SEQUENCE DESCRIPTION: SEO ID NO: 66: AGTAAATAAA AAGTTTGCTT TATTAAATTA TGTTTAGATA GTGSTTATAG TGCTTTACCC CTTCAAAATA GTAACTTCTA TCAATCATTT AGGATGTGTG TCAGACTATT CTGTGTCCTT 120 TAAGTGTGTK AACTAGTTTT AACCCTCTGC AAATATCTGA GGT ATG CTC TTT TTA Met Leu Phe Leu -25CAG ATG GGA AAA CAA TCT TGG ACT TTA ATA TTT TTT CTT AAT GTT ACA Gln Met Gly Lys Gln Ser Trp Thr Leu Ile Phe Phe Leu Asn Val Thr -15 CAA TTA GTA AGA GGC AGG GGG CCA GGC GGA CGG 256 Gin Leu Val Arg Gly Arg Gly Pro Gly Gly Arg

(2) INFORMATION FOR SEQ ID NO: 67:	
(i) SEQUENCE CHARACTERISTICS:  (A) LENGTH: 126 base pairs  (B) TYPE: NUCLEIC ACID  (C) STRANDEDNESS: DOUBLE  (D) TOPOLOGY: LINEAR	
(ii) MOLECULE TYPE: CDNA	
<pre>(vi) ORIGINAL SOURCE:     (A) ORGANISM: Homo Sapiens     (F) TISSUE TYPE: Brain</pre>	
<pre>(ix) FEATURE:     (A) NAME/KEY: sig_peptide     (B) LOCATION: 1999     (C) IDENTIFICATION METHOD: Von Heijne matrix     (D) OTHER INFORMATION: score 7.2</pre>	
(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 67:	
AATTGATTAG GAGATTAT ATG GAG CTG CGG GAS NTG CCG CCT GGG GGA AGA Met Glu Leu Arg Xaa Xaa Pro Pro Gly Gly Arg -25 -20	51
GAG GTG CAG CTT CTG CTA GGT TTG TGC TCT CCT CCC AGS RTC TCC TTG Glu Val Gln Leu Leu Gly Leu Cys Ser Pro Pro Xaa Xaa Ser Leu -15	99
GCT TCC TTC CCC AAA GCA GCT CAG ATG Ala Ser Phe Pro Lys Ala Ala Gln Met 1 5	126
(2) INFORMATION FOR SEQ ID NO: 68:	
<ul> <li>(i) SEQUENCE CHARACTERISTICS:</li> <li>(A) LENGTH: 117 base pairs</li> <li>(B) TYPE: NUCLEIC ACID</li> <li>(C) STRANDEDNESS: DOUBLE</li> <li>(D) TOPOLOGY: LINEAR</li> </ul>	
(ii) MOLECULE TYPE: CDNA	
<pre>(vi) ORIGINAL SOURCE:    (A) ORGANISM: Homo Sapiens    (F) TISSUE TYPE: Brain</pre>	
<pre>(ix) FEATURE:     (A) NAME/KEY: sig_peptide     (B) LOCATION: 4687     (C) IDENTIFICATION METHOD: Von Heijne matrix     (D) OTHER INFORMATION: score 7     seq LWSLLSSSGSHFG/IP</pre>	

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 68:

AGCAGGCCTT TGGGAGAGAA ACCTAATGCC TAAGCCTCAT CCTTT ATG CTC TGG TCT Met Leu Trp Ser	57
CTT CTT TCC TCT TCA GGC TCA CAT TTT GGT ATC CCT CAC CAC ACA TTT Leu Leu Ser Ser Gly Ser His Phe Gly Ile Pro His His Thr Phe -10 -5 1 5	105
CCC CAA GAA GGG Pro Gln Glu Gly 10	117
(2) INFORMATION FOR SEQ ID NO: 69:	•
(i) SEQUENCE CHARACTERISTICS:  (A) LENGTH: 445 base pairs  (B) TYPE: NUCLEIC ACID  (C) STRANDEDNESS: DOUBLE  (D) TOPOLOGY: LINEAR	
(ii) MOLECULE TYPE: CDNA	
<pre>(vi) ORIGINAL SOURCE:     (A) ORGANISM: Homo Sapiens     (F) TISSUE TYPE: Brain</pre>	
<pre>(ix) FEATURE:     (A) NAME/KEY: sig_peptide     (B) LOCATION: 110265     (C) IDENTIFICATION METHOD: Von Heijne matrix     (D) OTHER INFORMATION: score 7</pre>	
seq SVWLCLLCYFAFP/FQ	
(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 69:	
ATGCACCATG ATATTTTAT ACACGTTGTG TTAACTACTG TAAACACATT GTCTTCTTTA	60
TATTTCTTTG CAGGAAGTTC AGAAAAAAGT GTCACGTTTT AATCTGCAG ATG GAC ATA Met Asp Ile -50	118
AGT GGA TTA ATT CCT GGT CTA GTG TCT ACA TTC ATA CTT TTG TCT AKH Ser Gly Leu Ile Pro Gly Leu Val Ser Thr Phe Ile Leu Leu Ser Xaa -45 -35	166
Ser Gly Leu Ile Pro Gly Leu Val Ser Thr Phe Ile Leu Leu Ser Xaa	166 214
Ser Gly Leu Ile Pro Gly Leu Val Ser Thr Phe Ile Leu Leu Ser Xaa -45 -40 -35  AGT GAT CAC TAC GGA CGA AAA TTC CCT ATG ATT TTG TCT TCC GTT GGT Ser Asp His Tyr Gly Arg Lys Phe Pro Met Ile Leu Ser Ser Val Gly	
Ser Gly Leu Ile Pro Gly Leu Val Ser Thr Phe Ile Leu Leu Ser Xaa -45 -40 -35  AGT GAT CAC TAC GGA CGA AAA TTC CCT ATG ATT TTG TCT TCC GTT GGT Ser Asp His Tyr Gly Arg Lys Phe Pro Met Ile Leu Ser Ser Val Gly -30 -25 -20  GCT CTT GCA ACC AGC GTT TGG CTC TGT TTG CTT TGC TAT TTT GCC TTT Ala Leu Ala Thr Ser Val Trp Leu Cys Leu Leu Cys Tyr Phe Ala Phe	214

V	VO 99	7/0655	2						5	3					rei	111111111
Asn	Tyr	Thr	Thr	Fritze	1:;	Gly	Ala	Cys	Phe 25	Ala	Tyr	He	Val	Asp 30	Gln	
					CAA Gln											406
					ACT Thr											445
(2)			EQUEI (A) (B) (C)	NCE ( LEN( TYP! STR/	SEQ CHARA GTH: E: NO ANDEL OLOGY	ACTE 244 JCLE DNES	RIST: base IC AC S: DC	ICS: e pa: CID DUBL								
			ORIG (A)	INAL ORG	TYPI SOUI ANISI SUE	RCE: M: H	omo:	-	ens							
		i×)	(A) (B) (C) (D)	NAM LOC. IDE OTH	E/KE' ATIO NTIF ER II	N: 1 ICAT NFOR	37 ION :	226 METH ON:	OD: sco seq	re 7 LFV	ILLI					
	(	xi)	SĒQU	FILCE	DES	CRIP	TION	: SE	Q ID	NO:	70:					•
ACT	тттт	'GAA	TTTG	TTGC	TG G	TACA	GTTG	C AT	GTAT	TCTC	TTA	IAAAI	TAT	TTTG	AGGCC'	T 60
CAT	ATCI	GGT	TAT	TCTC	CT T	TCTC	TTA	C TI	TATCI	TGCG	TGI	TTTT	ACC	TTTT	TTTCA	T 120
∌.A.C	TAAC	STTT	TTGF	1					he S					he C	SAA ATG Slu Me -20	
				ı Let					e Lei					Let	A ATC	220
TTT	TG	r TC	r ct.	V TAC	GTO	G GCC	G CG1	Γ								244

244

L) INFORMATION FOR SEQ ID NO: 71:

Phe Cys Ser Let Tyr Val Ala Arg

- (1) SEQUENCE CHARACTERISTICS:
  (A) LUMGTH: 390 base pairs
  (B) 74 A: NUCLEIC ACID
  (C) URAMOFONESS: DOUBLE

(D) TOPOLOGY: LINEAR	
(ii) MOLECULE TYPE: CDNA	
<ul><li>(vi) ORIGINAL SOURCE:</li><li>(A) ORGANISM: Homo Sapiens</li><li>(F) TISSUE TYPE: Brain</li></ul>	
<pre>(ix) FEATURE:     (A) NAME/KEY: sig_peptide     (B) LOCATION: 289357     (C) IDENTIFICATION METHOD: Von Heijne matrix     (D) OTHER INFORMATION: score 6.9</pre>	
(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 71:	
AAGTACAAAG CCTACTCCAA AGACTGCAGC TTGAAGATAA AAGAGAGCAC TGCGTCCTTT	60
TGAAAATAAA GGCAGACACA AAGAAGAAAG GAGCTACCTT ACCCCAGCAT ATACCTGCGG	120
GATGTTCTCT CCAGTTCATT TTTACCTGGT GTCTTGAAAT CCGAGCAATT CCTAAAAAGG	180
CATTTTTGCG AGCCCTTGTG GACTATACCA GTGACAGTGC TGAAAAGCGC AGGCTACAGG	240
AGCTGTGCAG TAAACAAGGG GCAGCCGATT ATAGCCGCTT TGTACGAG ATG CCT GTG Met Pro Val	297
CCT GCT TGT TGG ATC TCC TCC TCG CTT TCC CTT CTT GCC AGC CAC Pro Ala Cys Trp Ile Ser Ser Ser Leu Ser Leu Leu Ala Ser His His -20 -15 -10	345
TCA GTC TCC TGC TCG AAC ATC TTC CTA AAC TTC AAC CCA GAC CGG Ser Val Ser Cys Ser Asn Ile Phe Leu Asn Phe Asn Pro Asp Arg 1 5 10	390
(2) INFORMATION FOR SEQ ID NO: 72:	
(i) SEQUENCE CHARACTERISTICS:  (A) LENGTH: 374 base pairs  (E) TYPE: NUCLEIC ACID  (C) STRANDEDNESS: DOUBLE  (D) TOPOLOGY: LINEAR	
(ii) MOLECULE TYPE: CDNA	
<ul><li>(vi) ORIGINAL SOURCE:</li><li>(A) ORGANISM: Homo Sapiens</li><li>(F) TISSUE TYPE: Brain</li></ul>	
<pre>(ix) FEATURE:     (A) NAME/KEY: sig_peptide</pre>	
(3) LOCATION: 198260	

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 72:

(D) OTHER INFORMATION: score 6.9

(C) IDENTIFICATION METHOD: Von Heijne matrix

seq LLACGSLLPGLWQ/HL

ATATATTTCT GAGGCAGTAC CCATCTCAUT TGTAAACTTA AAAGACACCG CAGAGATTTG	60
AGGGACTCAG AAGTCAAATA GAGTAGGTTA AAAACCTCTT ATTTTTCAAA TTAATTGTTT	120
TAAGAAACAA GCATACCTGT GTAAGTGAAA TATCTTAATT TGTGTTGAAT CAAGTTAGGA	180
GACAGAGATT CTCATGA ATG TGT CCT GTG TTC TCA AAG CAG CTG CTA GCC Met Cys Pro Val Phe Ser Lys Gln Leu Leu Ala -20 -15	230
TGT GGG TCT CTC CTA CCT GGG TTA TGG CAG CAC CTC ACA GCC AAT CAC Cys Gly Ser Leu Leu Pro Gly Leu Trp Gln His Leu Thr Ala Asn His -10 5	278
TGG CCT CCA TTC TCC SCT TTC CTC TGT ACA GTT TGC TCT GGT TCC TCA Trp Pro Pro Phe Ser Xaa Phe Leu Cys Thr Val Cys Ser Gly Ser Ser 10 15 20	326
GAG CAG ATT TOO GAG TAT ACT GCT TOA GCC ACG CCC CCA CTG TGC CTG Glu Gln Ile Ser Glu Tyr Thr Ala Ser Ala Thr Pro Pro Leu Cys Leu 25 30 35	374
(2) INFORMATION FOR SEQ ID NO: 73:  (i) SEQUENCE CHARACTERISTICS:  (A) LENGTH: 416 base pairs (B) TYPE: NUCLEIC ACID (C) STRANDEDNESS: DOUBLE (D) TOPOLOGY: LINEAR  (ii) MOLECULE TYPE: CDNA  (vi) ORIGINAL SOURCE: (A) ORGANISM: Homo Sapiens (F) TISSUE TYPE: Brain  (ix) FEATURE: (A) NAME/KEY: sig_peptide (B) LOCATION: 33260 (C) IDENTIFICATION METHOD: Von Heijne matrix (D) OTHER INFORMATION: score 6.9 seq LLPLSAWPPWAWH/HH  (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 73:	
ACGCTCAGCA GGRCCACTCC CGTGTTCCGG TC ATG GCT TTA ACA ATT CAT GGG  Met Ala Leu Thr Ile His Gly  -75  -70	53
GAA AGA ATG TO CCC GAT TGG GAG AGC CCC TGG ATC ACG TCT TCC CAA Glu Arg Met Frei Pro Asp Trp Glu Ser Pro Trp Ile Thr Ser Ser Gln -65 -60 -55	101
GCT CAG TCC 1.1 FCT CTT GGA GGG AGT CCG TCC TCG AGG GGC CCT CTG Ala Gln Ser U. Her Leu Gly Gly Ger Pro Ser Ser Arg Gly Pro Leu +45 -40	149

	CCC Pro															197
CAC His	AGC Ser -20	CAC His	CTG Leu	CTC Leu	CCC Pro	CGC Arg ~15	TCC Ser	CTC Leu	CTT Leu	CCC Pro	TTG Leu -10	TCA Ser	GCA Ala	TGG Trp	CCA Pro	245
CCG Pro -5	TGG Trp	GCC Ala	TGG Trp	CAT His	CAC His 1	CAT His	GGG Gly	CCT Pro	GGC Gly 5	ACA Thr	CAG <sup>.</sup> Gln	TCC Ser	CTC Leu	GTG Val 10	GGC Gly	293
TGC Cys	CTT Leu	TGT Cys	GCC Ala 15	ATG Met	AGC Ser	CCA Pro	CTG Leu	CTG Leu 20	CCG Pro	ACT Thr	CAC His	CTG Leu	TCC Ser 25	CTC Leu	CCA Pro	341
GTA Val	CTG Leu	GAA Glu 30	CCT Pro	TCT Ser	GGA Gly	ACA Thr	CCA Pro 35	GCA Ala	CTA Leu	AAA Lys	GAT Asp	AGG Arg 40	AGG Arg	CCC Pro	TGT Cys	389
	GTT Val 45													•		416
	(,	ii) i vi) ( ix)	(A) (B) (C) (D) MOLECORIG (A) (F) FEAT (A) (B) (C) (D)	TYPI STRU TOPO CULE INAL ORGA TIS: NAM LOC. IDE OTH	STH: E: NU ANDER DLOG'  TYP: SOU: ANISI SUE ' E/KE' ATION NTIF ER I	295 JCLE: DNESS Y: L: E: C RCE: M: HO TYPE Y: S N: 1 ICAT NFOR	base IC AC S: DO INEAL DNA  omo : Bra ig_pa 12 ION   MATI	e pai CID CUBLE Sapic ain eptic 86 METHO	ens de OD: sco seq	re 6 ILI	.8 ASSL	PTLS				
AAG	SAGTO															49
					-90					-85			-	Val	-80	
					/ Pro					Glu					AGG Arg	97
															GGA Gly	145

WO 99/06552		57	PC	T/IB98/01236
60	-55	,	-50	
GGC GAC GGC MAA GGA AA Gly Asp Gly Arg Gly As -45	TTC AAC CCC n Phe Asn Pro -40	Met Asn Phe Le	TG GTT GCG GGG eu Val Ala Gly 35	193
ACA TTT GCC TCC TCC TG Thr Phe Ala Ser Ser Cy -30	C CAC TCA CCA s His Ser Pro -25	CCT CTG CTC TO Pro Leu Leu Ti -20	GG TCC CTC CCT rp Ser Leu Pro	241
CCA AGA ATC CTC ATA GC Pro Arg Ile Leu Ile Al -15	a Ser Ser Leu			289
CCT GGG Pro Gly				295
(2) INFORMATION FOR SE	Q ID NO: 75:			
(B) TYPE:	: 361 base pa NUCLEIC ACID EDNESS: DOUBI	irs		
(ii) MOLECULE TY	PE: CDNA			
	URCE: SM: Homo Sapi TYPE: Brain	ens		
(B) LOCATI (C) IDENTI	EY: sig_pepti ON: 101187 FICATION METI INFORMATION:	HOD: Von Heijne		
(xi) SEQUENCE DE	SCRIPTION: S	EQ ID NO: 75:		
ACTOTOCOCT CCCCTCCCCG	GCACTGCAGC A	CCAGCCGTC TGCAG	CTCCG GCCGCCACT	T 60
GCGCCTCTCC AGCCTCCGCA	GCCCAACCGC C		CC AGC ACC ATT	115
TCC GCC TAC AAG GAG AM Ser Ala Tyr Lys Glu Ly -20				163
TGC TCC TGC UTC TAC ACCESS Ser Cys Fact Tyr Ti				211

GGG GAC ATG GEG GTG AAG CAG CTG GAC AAG CGG GCC TCA GGC CAG AGC Gly Asp Met Gln Val Lys Gln Leu Asp Lys Arg Ala Ser Gly Gln Ser 10

									,	U						
TTC Phe 25	GAG Glu	GTC Val	ATC Ile	CTC Leu	AAG Lys 30	TCC Ser	CCT Pro	TCT Ser	GAC Asp	CTG Leu 35	TCC Ser	CCA Pro	GAG Glu	AGC Ser	CCT Pro 40	307
					CCC Pro											355
	AAG Lys															361
(2)	( :	i) SE	EQUEN (A) (B) (C) (D)	ICE C LENG TYPE STRA TOPO	SEQ CHARA TH: C: NU NDED DLOGY	CTER 361 CLEI NESS	DASE C AC DO	CS: pai								·
	( -	vi) (	(A)	ORG	SOUF NISM SUE I	l: Ho			ens							
	(.	ix) !	(A) (B) (C)	NAME LOCA IDE	E/KEY ATION NTIFI ER IN	l: 2. CATI	$.\overline{3}43$	B METH(	DD: T	re 6.						
	(	xi)	SEQU	ENCE	DESC	CRIP	rion:	: SE	Q ID	NO:	76:					
				al T					al T					rg S	GC ACT er Thr 100	49
				Pro	TAT Tyr				Asn					Lys		97
			Arg					Glu					Thr		GTA Val	145
AAC Lys	S TCA S Ser -65	Ile	AGA : Arç	ACA Thr	CAG Gln	ACT Thr	Asp	TTC Phe	TAT	GCA Ala	ACA Thr	Lys	CCT	AAG Lys	AAG Lys	193
	As					His					. Leu				GAT Asp -35	241

CAG CAA TAT TTG TTC AGC CCA AGT AGA GAA ATG CCT ACT TTT TCA GGT Gln Gln Tyr Lau Phe Ser Pro Ser Arg Glu Met Pro Thr Phe Ser Gly

PCT/IB98/01236

Thr Leu Glu Gly -15	His Let 1	TT CCT ATO En Pro Me -1		CTT TTA Leu Leu	GGA CAA . Gly Gln : -5	ACC 337 Thr
CAA AGT AAT AGT Gln Ser Asn Ser l						361
(2) INFORMATION	FOR SEQ I	D NO: 77:				
(A) (B) (C)	NCE CHARAC LENGTH: 3 TYPE: NUC STRANDEDN TOPOLOGY:	88 base pa LEIC ACID ESS: DOUB	airs			
(ii) MOLE	CULE TYPE:	CDNA				
(A)	INAL SOURCE ORGANISM: TISSUE TY	Homo Sap	iens			
(B) (C)	URE: NAME/KEY: LOCATION: IDENTIFIC OTHER INF	8361 CATION MET	HOD: Von Hood Score 6.			
/ : \ 0.500	ENCE DESCE	RIPTION: S	FO ID NO-	77.		
(XI) SEQU	ENCE DESCR			,,.		
AGCAGAC ATS TOT		GAA ATC AG	T GGA ATG	ATA ATG		
AGCAGAC ATS TOT	GTA CTT ( Val Leu ( -115	GAA ATC AG Glu Ile Se ATA GGA TA	T GGA ATG r Gly Met -11 C CAG ATT	ATA ATG Ile Met O	Asn Arg	Val -105 GTC 97
AGCAGAC ATG TOT Met Ser	GTA CTT (CT Val Leu (CT Val Leu (CT Val Leu (CT Val Leu (CT Val	GAA ATC AG Glu Ile Se ATA GGA TA Ile Gly Ty ACT CCA TI	T GGA ATG r Gly Met -11 C CAG ATT r Gln 11e -95 T GTT TTC e Val Phe	ATA ATG Ile Met 0  TTT GGA Pne Gly  CGA CTT	Asn Arg  AAT GCA Asn Ala -90  TCT CAA	Val -105 GTC 97 Val GCT 145
AGCAGAC ATG TOT Met Ser  AAC AGC CAT ATA Asn Ser His Ile  TCT CTC ATA CTC Ser Leu lie Lee	GTA CTT (CT Val Leu (CT -115) CCA GGA APPRO Gly CT -100 GGGT TTA APPRO Gly Leu CT	GAA ATC AG Glu Ile Se  ATA GGA TA Ile Gly Ty  ACT CCA TT Ihr Pro Ph  -8  ACA GCA CA	T GGA ATG r Gly Met -11 C CAG ATT r Gln Ile -95 T GTT TTC te Val Phe 0	ATA ATG Ile Met 0  TTT GGA Pne Gly  CGA CTT Arg Leu  TCA GAA	AAT GCA ASN Ala -90 TCT CAA Ser Gln -75 CTT TAT	Val -105 GTC 97 Val GCT 145 Ala GTG 193
AGCAGAC ATG TOT Met Ser  AAC AGC CAT ATA Asn Ser His Ile  TCT CTC ATA CTC Ser Leu Ile Leu -85  ACA GAC TTG GAR Thr Asp Leu Gle	GTA CTT CO TVAL Leu CO -115  CCCA GGA A Pro Gly CO -100  GGGT TTA A GIY Leu CO GIY Ser Asn	GAA ATC AG Glu Ile Se  ATA GGA TA Ile Gly Ty  ACT CCA TT Thr Pro Ph  -8  ACA GCA CA Thr Ala Hi  -65	T GGA ATG r Gly Met -11 C CAG ATT r Gln Ile -95 T GTT TTC e Val Phe 0 AT TCT GCT s Ser Ala	ATA ATG Ile Met 0  TTT GGA Pne Gly  CGA CTT Arg Leu  TCA GAA Ser Glu -60	ASN Arg  AAT GCA ASN Ala -90  TCT CAA Ser Gln -75  CTT TAT Leu Tyr  ATG GTT	Val -105 GTC 97 Val GCT 145 Ala GTG 193 Val
AGCAGAC ATG TOT Met Ser  AAC AGC CAT ATA ASS Ser His Ile  TCT CTC ATA CTC Ser Leu Ile Leu -85  ACA GAC TTG GAM Thr Asp Lou Glu-70  ATT GCA TTT GGT Ile Ala Eng Glu-	GGTA CTT (CVal Leu CVal Leu CVal Leu CVal Leu CVal CCA GGA A Pro Gly CVal CVal CVal CVal CVal CVal CVal CVal	GAA ATC AG GIU Ile Se  ATA GGA TA Ile GIY TY  ACT CCA TI Thr Pro Ph  -8  ACA GCA CA Thr Ala Hi  -65  GAA GAT GT Glu Asp Va  -50  GTG TCT CT	T GGA ATG r Gly Met -11 C CAG ATT r Gln Ile -95 T GTT TTC te Val Phe 0 AT TCT GCT as Ser Ala CC ATA GTT al Ile Val	ATA ATG Ile Met  O  TTT GGA Pne Gly  CGA CTT Arg Leu  TCA GAA Ser Glu -60  CTT TCT Leu Ser -45  G ATT TTC Flie Phe	Asn Arg  AAT GCA Asn Ala -90  TCT CAA Ser Gln -75  CTT TAT Leu Tyr  ATG GTT Met Val  TTT TTT	Val -105  GTC 97 Val 97  GCT 145 Ala 193 Val 111e  TTG 289

Leu	TTT Phe	GGA Gly	CAT His -5	TTA Leu	<b>A</b> CA Thr	TCT Ser	GCA Ala	AGG Arg 1	AGG Arg	GCT Ala	CGA Arg	AAA Lys 5	TCT Ser	GAG Glu	GTT Val	385
CCT Pro																388
(2)	INFO	RMAT	ІОИ	FOR	SEQ	ID N	0: 7	8:								
	(i		QUEN (A) : (B) : (C) :	LENG TYPE STRA	TH: : NU NDED	291 CLEI NESS	base C AC : DO	pai ID UBLE								
	(i	i) M	OLEC	ULE	TYPE	: CD	NA									
	( v	i) O	RIGI (A) (F)	ORGA	NISM	: Ho		•	ns						·	
	(i	×) E	(C)	NAME LOCA IDEN	TION TIFI	: 79	28 ON M	5 ETHO	D: V	on H	leijn 7	e ma	trix			
									seq	FFKL	LLLG	AMCS	G/AR			
	( 8	:i) S	EQUE	NCE	DESC	RIPT	'ION :	SEC	_			AMCS	G/AR			
AAG.									) ID	NO:	78:				SAGTGT	60
		GA C	CTGGA	LAGAC	G AG	GAAAG TGT	aact aaa	GGC	ID ATGC:	NO: TTGT AAA	78: AAC	GCCC	GGG F	\TGGG	TGT	60 111
ATTO	ACTO	GA CTT 1	CTGGAA CTG	LAGAC NGAT GGA	ATG Met	TGT Cys	AAA Lys GCC	GGC Gly	ATGC: ATT Ile -65	NO: FTGT AAA Lys AGA	78: AACC GCT Ala	GGCCC GGT Gly TGT	GGG AGASP	ACC Thr -60	TGT Cys ATG	
GAG Glu GCT	ACTGT CCTTT AAG	GA CTT TC	CTGGA TTGAA GTG Val -55	AGAC AGAT GGA Gly TTT	ATG Met TAT Tyr	TGT Cys TCT Ser	GCC Ala	GGC Gly GTG Val -50	ATT Ile -65 TAT Tyr	NO: FTGT AAA Lys AGA Arg	78: AACC GCT Ala GTC Val	GGCCG GGT Gly TGT Cys	GGG ASP TTT Phe -45	ACC Thr -60 GGA Gly	TGT Cys ATG Met	111
GAG Glu GCT Ala	ACTOTO CCTTT AAG Lys TGT	CTG CTG Leu TTC Phe -40 AGT	GTG Val -55 TTC Phe	AGAC GGA Gly TTT Phe	ATG Met TAT Tyr ATC Ile	TGT Cys TCT Ser TTC Phe	GCC Ala TGT Cys -35	GGC Gly GTG Val -50 CTA Leu	ATT Ile -65 TAT Tyr CTG Leu	NO: TTGT AAA Lys AGA Arg ACC Thr	78: AACC GCT Ala GTC Val TTG Leu	GGCCCC GGT Gly TGT Cys AAA Lys -30	GGG ASP TTT Phe -45 ATC Ile	ACC Thr -60 GGA Gly AAC Asn	TGT Cys ATG Met AAC Asn	111

- (2) INFORMATION FOR SEQ ID NO: 79:
  - (1) SEQUENCE CHARACTERISTICS:

			(B)	) TYI	PET 1 RANDE	AUCL:	EIC Z SS: I	DOURI								
		(ii)	MOLE	ECULE	E TYE	PE: (	CDNA									
	(	(vi)	(A)	GINAI ORG TIS	SANIS	M: F	omo	Sapi ain	.ens							
	(	ix)	(A) (B) (C)	TOC	E/KE ATIO NTIF	N: 6 ICAT	13 ION	METH	OD: sco	re 6	. 6		natri 'WA/Q			
	(	xi)	SEQU	ENCE	DES	CRIP	TION	: SE	Q ID	NO:	79:					
ATT	TTCC	CGG	GTCT	TCTC	CA G	CTGC	CACC	G CT	TTAC	TGCA	AAA .	.CTGA	.CGG	GCGC	'AAAAAC	60
ATG	AGT	GAC	TCC	GCG	GGA Gly	GGG	CCC	GCT Ala	CCM	CTC Leu					AAG Lys	108
CTC Leu	CCA Pro	GTG Val	TGG Trp -85	GTG Val	GTG Val	GAG Glu	GAT Asp	CAT His -80	CAG Gln	GAG Glu	GTT Val	CTA Leu	CCC Pro	TTT Phe	ATA Ile	156
TAC Tyr	уrд	GCC Ala -70	ATA Ile	GGC Gly	TCA Ser	AAG Lys	CAT His	CTT Leu	CCT Pro	GCC Ala	AGT Ser	AAT Asn -60	GTA Val	AGT Ser	TTT Phe	204
TTA Leu	CAT His -35	TTC Phe	GAC Asp	TCA Ser	CAT His	CCA Pro -50	GAC Asp	CTC Leu	CTT Leu	ATT Ile	CCT Pro -45	GTG Val	AAT Asn	ATG Met	CCA Pro	252
GCA Ala -40	GAC Asp	ACC Thr	GTG Val	TTT Phe	GAT Asp -35	AAG Lys	GAA Glu	ACA Thr	CTC Leu	TTT Phe -30	GGA Gly	GAA Glu	TTA Leu	AGT Ser	ATT Ile -25	300
GAA Glu	AAT Asn	TGG Trp	ATT Ile	ATG Met -20	CCT Pro	GCA Ala	GTT Val	TAT Tyr	GCT Ala -15	GGC Gly	CAT His	TTT Phe	TCA Ser	CAT His	GTA Val	348
GTA Val	TGG Tip	TTT Phe	CAT His	CCC Pro	ACA Thr	TGG Trp	GCT Ala	CAG Gln 1	CAG Gln	ATC Ile	AGA Arg	GAG Glu 5	GGC Gly	AGA Arg	CAC His	396
CAC																402

(2) IUFORMATION FOR SEQ ID NO: 80:

(L) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 338 base pairs

v	VO 99	/0655	2						62	2			PC	T/IB98/0
			(C)	TYPE STRA TOPO	NDED	NESS	: DO	UBLE						
	(i	i) M	OLEC	ULE	TYPE	: CD	NA							
	( v	i) O	(A)	NAL ORGA TISS	NISM	: Но			ns					
	·	x) F	(A) (B) (C) (D)	RE: NAME LOCA IDEN OTHE	TION TIFI R IN	: 12 CATI FORM	15 ON M ATIO	2 ETHC N:	D: V scor seq	e 6. SSCV	3 LLTA			
	(,	.1) 3	EQUE	NCE	DESC	KIFI	ION:	SEC	, 10	NO:	80:			
<u>aaai</u>	ACGCC	STG A				Cys					Val		CTC Leu	50
	GTG Val													98
	GGC Gly													146
	GCC Ala													194
	TGG Trp													242
	AGT Ser													290
	ANN Xaa								Lys					338

# (2) INFORMATION FOR SEQ ID NO: 81:

- (i) SEQUENCE CHARACTERISTICS:
  - (A) LENGTH: 229 base pairs
  - (3) TYPE: NUCLEIC ACID
  - (C) STRANDEDNESS: DOUBLE
  - (D) TOPOLOGY: LINEAR
- (ii) MOLECULE TYPE: CDNA
- (vi) ORIGINAL SOURCE:

(A) ORGANISM: Homo Sapiens (F) TISSUE TYPE: Brain

(ix) FEATURE:

(A) NAME/KEY: sig\_peptide

- (B) LOCATION: 14..139
- (C) IDENTIFICATION METHOD: Von Heijne matrix
- (D) OTHER INFORMATION: score 6.1

seq DLAVALSLLPAWT/ES

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 81:

ATTAAAGTCA AAG ATG ATT ATT CCT TTC AAA ATA AAG AAT CTA GGA GGG Met Ile Ile Pro Phe Lys Ile Lys Asn Leu Gly Gly 49 -40

CGA GTC CTG CTG TCG GGA AGG GAG ATG TTT CCT GCT TCC GTC CGT GCT Arg Val Leu Leu Ser Gly Arg Glu Met Phe Pro Ala Ser Val Arg Ala 97 -25 -20

CCT GAC CTG GCG GTG GCC CTG TCC CTG CTA CCT GCG TGG ACA GAG TCT Fro Asp Leu Ala Val Ala Leu Ser Leu Leu Pro Ala Trp Thr Glu Ser 145 -10 - 5

CCA ACA CGC GGC AGC CAC CAG AGC CAG GCC CGA GCG CAC AGC CGT GCA Pro Thr Arg Gly Ser His Gln Ser Gln Ala Arg Ala His Ser Arg Ala 10

TTG CGA AAG CAA AGC CGA AAC ACG AGG TCG CCC CGG Leu Arg Lys Gln Ser Arg Asn Thr Arg Ser Pro Arg 229 20 25

# (2) INFORMATION FOR SEQ ID NO: 82:

- (i) SEQUENCE CHARACTERISTICS:
  - (A) LENGTH: 249 base pairs
  - (B) TYPE: NUCLEIC ACID
  - (C) STRANDEDNESS: DOUBLE
  - (D) TOPOLOGY: LINEAR
- (ii) MOLECULE TYPE: CDNA
- (vi) ORIGINAL SOURCE:
  - (A) ORGANISM: Homo Sapiens
  - (F) TISSUE TYPE: Brain
- (ix) FEATURE:
  - (A) NAME/KEY: sig\_peptide
  - (3) LOCATION: 70..228
  - (C) IDENTIFICATION METHOD: Von Heijne matrix
  - (D) OTHER INFORMATION: score 6

seq ALILLLLAQKGPS/XF

(mi) SEQUENCE DESCRIPTION: SEQ ID NO: 82:

GGTG	AATG	T AT Me	G GT t Va	G TG 1 Cy	T AG	r Al	T CC	T AG o Ar	A AA g Ly	A AT's Il	e Va	A GT l Va	T AG 1 Ar	G GC	A TTT a Phe -40	111
ATT Ile	ACG . Thr	ATA . Ile	Ile	TTC Phe -35	ATA Ile	TAT Tyr	TAT (	Ala	ATA Ile -30	AAG Lys	AAG Lys	AGG Arg	Ala	AAT ( Asn ( -25	GAA Glu	159
CCT Pro	GCA (	Ala '	TAT Tyr -20	TTG Leu	ATG Met	TTG Leu	Lys	CCT Pro -15	GAG Glu	GCT Ala	CTG Leu	Ile	CTC Leu -10	CTT (	CTG Leu	207
					CCC . Pro											249
(2)		) SE	QUEN (A) (B) (C)	CE C LENG TYPE STRA	SEQ CHARA CHH: NU NDED DLOGY	CTER 289 CLEI NESS	ISTI base C AC : DO	CS: pai ID UBLE							·	
	(i	i) M	OLEC	ULE	TYPE	: CD	NA									
	(v		(A)	ORGA	SOUR NISM SUE T	: Ho			ns							
	(i	x) F	(A) (B) (C)	NAME LOCA IDEN	E/KEY ATION NTIFI ER IN	: 11 CATI	02 ON M	29 ETHO	D: V		9					
	( x	:i) S	EQUE	NCE	DESC	RIPT	: NOI	SE(	O I D	NO:	83:					
ACCO	CTGCI	GG G	CGGC	SAAG	GC GC	CGC	CCCG	CC	GAGG'	TGGC	GGC	GGCT	CCT (	CAGAT	GGGAG	60
AAGA	AGT1	GT C	CATO	STTC.	AC AC	CTGG	gtga <i>i</i>	A GG	AAGC'	TGAA	ACC	ACAG	Me		T GAG ir Glu	118
TCC Ser	TCC Ser	ATG Met -35	AAG Lys	AAG Lys	CTG Leu	GCC Ala	TCC Ser -30	ACC Thr	CTG Leu	CTG Leu	GAC Asp	GCC Ala -25	ATC Ile	ACC Thr	GAT Asp	166
AAG Lys	GAC Asp -20	CCC Pro	CTG Leu	GTG Val	CAG Gln	GAG Glu -15	CAG Gln	GTC Val	TGC Cys	AGT Ser	GCC Ala -10	Leu	TGC Cys	TCC Ser	CTC · Leu	214
303 31y -3	Glu	GTG Val	CGG Arg	Pro	VTG Xaa 1	GAG Glu	ACG Thr	CTC Leu	CGT Arg	Ala	TGC Cys	GAG Glu	GAG Glu	TAT Tyr 10	CTG Leu	262
203	CAS	ATG	ACA	AGC	TGG	CAC	ACC	CGG	į							299

And Maa Met Th: Ser Trp His Thr Arg

WO 99/06552

1.1	
(?) INFORMATION FOR SEQ ID NO: 84:	
(i) SEQUENCE CHARACTERISTICS:	
(A) LENGTH: 252 base pairs	
(B) TYPE: NUCLEIC ACID (C) STRANDEDNESS: DOUBLE	
(D) TOPOLOGY: LINEAR	
(ii) MOLECULE TYPE: CDNA	
(vi) ORIGINAL SOURCE:	
(A) ORGANISM: Homo Sapiens	
(F) TISSUE TYPE: Brain	
(ix) FEATURE:	
(A) NAME/KEY: sig_peptide	
<ul><li>(B) LOCATION: 76204</li><li>(C) IDENTIFICATION METHOD: Von Heijne matrix</li></ul>	
(D) OTHER INFORMATION: score 5.9	
seq VFLFHCTSGLSSC/KC	
(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 84:	
(AI) SEQUENCE DESCRIPTION. SEQ 15 No. 04.	
AGTARAACAA AAGGATATGC ACACACAT ATTTAAATAC ATGTAGTTTT TTGCATAAAT	60
TATCACTGAG AGGAA ATG CAA GAA ACT GAT TGT AAT AAA CGC TGG GGA AGG	111
Met Gln Glu Thr Asp Cys Asn Lys Arg Trp Gly Arg	
-40 -35	
GGC CTG GGT GGC CTG TGG TCA GAA ACA GGA AGG AGA TTT CAT TGC AAA	159
Gly Leu Gly Gly Leu Trp Ser Glu Thr Gly Arg Arg Phe His Cys Lys	
-30 -25 -20	
TOT TIT GTA TIT CIT TIT CAC TGT ACT TOT GGA TIA TOT TOA TGC AAA	207
Ser Phe Val Phe Leu Phe His Cys Thr Ser Gly Leu Ser Ser Cys Lys	
-15 -10 -5	
TGT TOT AAA AAG CAT TYM AAA TAT TGC TTC TGT TTT GTG GCA AGT	252
Cys Ser Lys Lys His Xaa Lys Tyr Cys Phe Cys Phe Val Ala Ser	
5 10 15	
A LANGUAGUA TON ODO TO NO OF	
(2) INFORMATION FOR SEQ ID NO: 85:	

- (1) SEQUENCE CHARACTERISTICS:
  - (A) LENGTH: 366 base pairs
    (B) TYPE: NUCLEIC ACID
    (C) STRANDEDNESS: DOUBLE
    (D) TOPOLOGY: LINEAR
- (ii) MOLECULE TYPE: CDNA
- (V1) ORIGINAL SOURCE:
  - (A) ORGANISM: Homo Sapiens

(F) TISSUE TYPE: Brain

ŧ	'n	x)	Į.	F	Δ:	ri	П	RΕ	

- (A) NAME/KEY: sig\_peptide
- (B) LOCATION: 232..282
- (C) IDENTIFICATION METHOD: Von Heijne matrix
- (D) OTHER INFORMATION: score 5.8

seq VPWLSSTVSCAQG/LR

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 85:

ATGAGTGGTC MGGAGATAAC ACTTAATGCT TTATTCTTAA GTGTTGGAAG GAGCAAGTAA GTGGTCTAGT GAGCTGTTTT TAGAGGAACT GTATAATATG TAACACATTG TCATTATATT CACTAACTCC CAAAGTATTC TTGAGATATT GANACAAAAC AAAGAGCTTG AATAGAAACC CTGAGCAACA ATGTATTTAC TTTCCACTTG CAGCAGAACT TGGCCTTTCA G ATG CTC Met Leu CTT GAA GTG CCT TGG CTT AGC AGT ACT GTC TCT TGT GCC CAG GGT CTG 285 Leu Glu Val Pro Trp Leu Ser Ser Thr Val Ser Cys Ala Gln Gly Leu -15 -10 AGA TTG GCA CAA CAC AGA GTG CCT TTC TTT TAT TCA AAT GTC TCA TTA Arg Leu Ala Gln His Arg Val Pro Phe Phe Tyr Ser Asn Val Ser Leu 10 TGC AAA TTA TTG CTG CCA GCC AMM CTG CAC GGG 366 Cys Lys Leu Leu Pro Ala Xaa Leu His Gly

### (2) INFORMATION FOR SEQ ID NO: 86:

- (i) SEQUENCE CHARACTERISTICS:
  - (A) LENGTH: 437 base pairs
  - (B) TYPE: NUCLEIC ACID
  - (C) STRANDEDNESS: DOUBLE
  - (D) TOPOLOGY: LINEAR
- (ii) MOLECULE TYPE: CDNA
- (vi) ORIGINAL SOURCE:
  - (A) ORGANISM: Homo Sapiens
  - (F) TISSUE TYPE: Brain
- (ix) FEATURE:
  - (A) NAME/KEY: sig\_peptide
  - (B) LOCATION: 123..209
  - (C) IDENTIFICATION METHOD: Von Heijne matrix
  - (D) OTHER INFORMATION: score 5.7

seq SPAFLAVAGPGWA/RP

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 86:

	wo	99/06:	552							67					PC'	T/IB98/012
GCT	TTA	ATTG	ATC	CTGC	TGC (	CCTCT	rggg,	NG CA	NCCC/	O7 NCACA	a nec	·,·, ·, ·, ·	neames.		CTGGACC	
TC	ATG	TCT	GGA	GGG	CGG Arg -25	n mc	0.00		_							120
					-25			.,,,,	nrg	-20	Ser	Gln	Gln	Ser	Thr -15	
		•		-10	)				-5	Pro	Gly	Trp	Ala	Arg	CCT Pro	215
		5			ACC Thr	•	10	2	201	GIN	Leu	Ala 15	Arg	His	Leu	263
	20				CCT Pro	25		****	neu	GIŸ	30	Leu	Val	Gln	Pro	311
35						_	1		Cly	45	vaı	Leu	Gly	Glu	Gly 50	359
GGG Gly				55				Gry	60	TGC Cys	CTC Leu	CAG Gln	TCG Ser	TGC Cys 65	TCC Ser	407
ACA (	GAC Asp	GTG Val	CTD Leu 70	ANG Xaa	CAT His	GTC Val	CTC Leu	CTG Leu 75	GCG Ala							437
(2) 1	INFO	RMAT	ІОИ	FOR	SEQ	ID N	0:8	7:								
	(i)	,	(A) ; (B) ; (C) ;	LENG' TYPE STRAI	HARAGIH: 4 : NUG NDEDN	137 b CLEIC NESS:	Dase DOI	pai:	cs							
	(ii	.) MC	LEC	JLE :	TYPE:	CDN	IA									
	(vi	(	A) (	RGAN	SOURC NISM: DE TY	Hom	o Sa Brai	pien n	ıs							
	(ix	) FE ( (	ATUR A) N B) L C) I	RE: IAME/ OCAT DENT	KEY: ION: IFIC INF	sig 63. ATIO	_pep .116 N MF	tide THOD : s	: Vo	5.6	ijne SFFP					
	(xi	) SE	QUEN	CE D	ESCR	IPTI	ON:									
AACTGT	rggt(	C AC	ATCC	CTCA	. AAA	GTGA	ACA	GTCG	CCAT	CG G	AGGG	ுருருரு	C C.	cc		
70 <b>2</b> 00	_ m/	~ ~.	~							0		O . I I	O GA	υ <b>UA</b> G	ACCS	60

Met Leu Gin Met Leu Trp His Phe Leu Ala Ser Phe Phe Pro Arg

-10

GCT GGG TGC CAC GGC TCC AGA GAG GGG GAC GAT CGT GAA GTC AGA GGC Ala Gly Cys His Gly Ser Arg Glu Gly Asp Asp Arg Glu Val Arg Gly 1 ACC CCA GCC CCT GCC TGG AGA GAC CAG ATG GCA AGC TTT TTG GGG AAA 203 Thr Pro Ala Pro Ala Trp Arg Asp Gln Met Ala Ser Phe Leu Gly Lys 15 20 CAG GAC GGA AGG GCT GAG GCC ACG GAA AAA AGA CCC ACC ATT TTG CTG 251 Gln Asp Gly Arg Ala Glu Ala Thr Glu Lys Arg Pro Thr Ile Leu Leu 35 GTG GTT GGA CCT GCA GAG CAG TTT CCT AAG AAA ATT GTA CAA GCT GGA Val Val Gly Pro Ala Glu Gln Phe Pro Lys Lys Ile Val Gln Ala Gly 50 GAT AAG GAC CTT GAT GGG CAG CTA GAC TTT GAA GAA TTT GTC CAT TAT 347 Asp Lys Asp Leu Asp Gly Gln Leu Asp Phe Glu Glu Phe Val His Tyr CTC CAA GAT CAT GAG AAG CTG AGG CTG GTG TTT AAG AGT TTG GAC 395 Leu Gln Asp His Glu Lys Lys Leu Arg Leu Val Phe Lys Ser Leu Asp 80 AAA AAG AAT GAT GGA CGC ATT GAC GCG CAG GAG ATC ATG CAG 437 Lys Lys Asn Asp Gly Arg Ile Asp Ala Gln Glu Ile Met Gln 100

### (2) INFORMATION FOR SEQ ID NO: 88:

- (i) SEQUENCE CHARACTERISTICS:
  - (A) LENGTH: 113 base pairs
  - (B) TYPE: NUCLEIC ACID
  - (C) STRANDEDNESS: DOUBLE
  - (D) TOPOLOGY: LINEAR
- (ii) MOLECULE TYPE: CDNA
- (vi) ORIGINAL SOURCE:
  - (A) ORGANISM: Homo Sapiens
  - (F) TISSUE TYPE: Brain
- (ix) FEATURE:
  - (A) NAME/KEY: sig\_peptide
  - (B) LOCATION:  $3..\overline{62}$
  - (C) IDENTIFICATION METHOD: Von Heijne matrix
  - (D) OTHER INFORMATION: score 5.6

seq SLVCLLAMGKGLG/SS

95

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 88:

AC ATG TAT TCC CAT CCC GTG TCC TCA CTG GTG TGT CTC CTG GCC ATG

Met Tyr Ser His Pro Val Ser Ser Leu Val Cys Leu Leu Ala Met

-20

-15

-10

GGC AAG GGA CTC GGG TCA TCC CAG GCC CTG GTC CAG CCA GAC ACC TGG
Gly Lys Gly Leu Gly Ser Ser Gln Ala Leu Val Gln Pro Asp Thr Trp

WO 99/06552		69		PCT/IB98/01236
-5	1	5		
CCC CAC ACC TCC (Pro His Thr Ser 15	CCG CGG Pro Arg	J	10	113
(2) INFORMATION E	FOR SEQ ID NO:	89:		
(A) L (B) T (C) S	CE CHARACTERIST LENGTH: 362 bas LYPE: NUCLEIC A TRANDEDNESS: D OPOLOGY: LINEA	e pairs CID OUBLE		
(ii) MOLECU	LE TYPE: CDNA			
(vi) ORIGIN (A) O (F) T	AL SOURCE: RGANISM: Homo ISSUE TYPE: Br	Sapiens ain		
(D) O. (C) II	AME/KEY: sig_po OCATION: 871 DENTIFICATION N THER INFORMATIO	91 METHOD: Von Heis	GSGAFS/EV	
AACAGACCTG TACGAGG	CTGG AGTGGGAGC	I CAAGCAGGAT TCT	TCCCGAG TCCCTGGC	AT 60
CCTCAGAAGC TTCAAC	ICTG GAGGCA ATO Met -35	- GIY Arg Lys Gl	A GAA GAT GAC TGG u Glu Asp Asp Cys -30	2 113
AGT DCC TGG AAG AA Ser Xaa Trp Lys Ly -25	AA CAG ACC ACC ys Gln Thr Thr -20	AAC ATC CGG AAA Asn Ile Arg Lys -15	ACC TTC ATT TTT Thr Phe Ile Phe	161
ATG GAA GTG CTG GC Met Glu Val Leu Gl -10	GA TCA GGA GCT Ly Ser Gly Ala -5	TTC TCA GAA GTT Phe Ser Glu Val 1	TTC CTG GTG AAG Phe Leu Val Lys 5	209
CAA AGA CTG ACT GG Gln Arg Leu Thr Gl 10	GG AAG CTC TTT Y Lys Leu Phe	GCT CTG AAG TGC Ala Leu Lys Cys 15	ATC AAG AAG TCA Ile Lys Lys Ser 20	257
CCT GCC TTC CGG GA Pro Ala Phe Arg As 25	C AGC AGC CTG p Ser Ser Leu 30	Giu Ash Glu Ile	GCT GTG TTG AAA Ala Val Leu Lys 35	305
AAG ATC AAG CAT GA Lys Ile Lys Eis Gl 40	A AAC ATT GTG u Asn Ile Val 45	ACC CTG GAG GAC Thr Leu Glu Asp 50	ATC TAT GAG AGC Ile Tyr Glu Ser	353
ACA CAA GGG Thr Gln Gly 55				362

(2) INFORMATION FOR SEQ ID NO: 90:	
(i) SEQUENCE CHARACTERISTICS:  (A) LENGTH: 384 base pairs	
(B) TYPE: NUCLEIC ACID (C) STRANDEDNESS: DOUBLE (D) TOPOLOGY: LINEAR	
(ii) MOLECULE TYPE: CDNA	
<pre>(vi) ORIGINAL SOURCE:     (A) ORGANISM: Homo Sapiens     (F) TISSUE TYPE: Brain</pre>	
<pre>(ix) FEATURE:     (A) NAME/KEY: sig_peptide     (B) LOCATION: 241327     (C) IDENTIFICATION METHOD: Von Heijne matrix     (D) OTHER INFORMATION: score 5.6</pre>	
(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 90:	
AAGCGGCGCA CCGGGHGAAG ATGGCGTTGG AGGTCGGCGA TATGGAAGAT GGGCAGCTTT	60
CCGACTCGGA TTCCGACATG ACGGTCGCAC CCAGCGACAG GCCGCTGCAA TTGCCAAAAG	120
TGCTAGGTGG CGACAGTGCT ATGAGGGCCT TCCAGAACAC GGCAACTGCA TGTGCACCAG	180
TATCACATTA TCGAGCTGTT GAAAGTGTGG ATTCAAGTGA AGAAAGTTTT TCTGATTCAG	240
ATG ATG ATA GCT GTC TTT GGA AAC GCA AAC GAC AGA AAT GTT TTA ACC Met Met Ile Ala Val Phe Gly Asn Ala Asn Asp Arg Asn Val Leu Thr -25 -20 -15	288
CTC CTC CCA AAC CAG AGC CTT TTC AGT TTG GCC AGA GCA GTC AGA AAC Leu Leu Pro Asn Gln Ser Leu Phe Ser Leu Ala Arg Ala Val Arg Asn -10 -5 1	336
CAC CTG TTG CTG GAG GAA AGA AGA TTA ACA ACA TAT GGG GTG CTG TGC His Leu Leu Clu Glu Arg Arg Leu Thr Thr Tyr Gly Val Leu Cys 5 10 15	384

# (2) INFORMATION FOR SEQ ID NO: 91:

- (i) SEQUENCE CHARACTERISTICS:
  - (A) LENGTH: 314 base pairs

  - (3) TYPE: NUCLEIC ACID
    (C) STRANDEDNESS: DOUBLE
  - (D) TOPOLOGY: LINEAR
- (ii) MOLECULE TYPE: CONA
- (vi) ORIGINAL SOURCE:
  - (A) ORGANISM: Homo Sapiens

(F) TISSUE TYPE: Brain

				JR	

- (A) NAME/KEY: sig\_peptide
- (B) LOCATION: 141..197
- (C) IDENTIFICATION METHOD: Von Heijne matrix
- (D) OTHER INFORMATION: score 5.6

seq LVVTAWFFGMCRS/KA

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 91:

ATCCCAGAAC ACCATTGGGA GAACGCCAGG ACACCGTGAA GGCTGAGCCG CCACTCGGTT 60

CTGATGCCGC ATCCATTGGT CAGTGCACGT TCTTTGAGCT TCCACTTGAG TGCACGTTCT 120

TTGAGCTTCC ACTTGAGTGC ATG TTC TTT GAG CTT CCA CTT GTA GTG ACT GCC 173

Met Phe Phe Glu Leu Pro Leu Val Val Thr Ala

-15

TGG TTC TTC GGG ATG TGC AGG AGC AAA GCG CTC TTA GGC AAT GCT CGT
Trp Phe Phe Gly Met Cys Arg Ser Lys Ala Leu Leu Gly Asn Ala Arg

TCT GCC CTG TGT TTA CAA ACC AAG GCC TGT GCC AGC TCT ACT CAG CCT 269
Ser Ala Leu Cys Leu Gln Thr Lys Ala Cys Ala Ser Ser Thr Gln Pro
10 15 20

GAC ACC CAT AAT GAG CAC CAT CCC AGG AAT CCC TGT CCC TAC TTG
Asp Thr His Asn Glu His His Pro Arg Asn Pro Cys Pro Tyr Leu
25 30 35

# (2) INFORMATION FOR SEQ ID NO: 92:

- (i) SEQUENCE CHARACTERISTICS:
  - (A) LENGTH: 316 base pairs
  - (B) TYPE: NUCLEIC ACID
  - (C) STRANDEDMESS: DOUBLE
  - (D) TOPOLOGY: LINEAR
- (ii) MOLECULE TYPE: CDNA
- (vi) ORIGINAL SOURCE:
  - (A) ORGANISM: Homo Sapiens
  - (F) TISSUE TYPE: Brain
- (ix) FEATURE:
  - (A) NAME/KEY: sig\_peptide
  - (B) LOCATION: 155..286
  - (C) IDENTIFICATION METHOD: Von Heijne matrix
  - (D) OTHER INFORMATION: score 5.5

seq FLLIVANVHFSQT/WV

(X1) SEQUENCE DESCRIPTION: SEQ ID NO: 92:

ATAAATAGCA TIGITTACAT CGACCAAATA TIGCCIGITI CCTITAATIC AAATBCATTA 60

HETTCCCGCC TOCCTCTCCT TCCCCGCCAT GTTGCTSTTT TAAGGCTTCA TATGTATTAA 120

CATTTCTCTG ATCAAAATTG TGGCTGTTTT CCTT ATG AAC CAT AAT ATA ATC ATT  Met Asn His Asn Ile Ile Ile -40	175
TGT GTG ATG TAC ATT GTG CCA TTT TTG ATG ACT AAA TGT CTA TAT TTC Cys Val Met Tyr Ile Val Pro Phe Leu Met Thr Lys Cys Leu Tyr Phe -35 -25	223
TGC CAT TCC TGT AAG AGA GGG AGT TTT TTA CTG ATA GTA GCA AAT GTT Cys His Ser Cys Lys Arg Gly Ser Phe Leu Leu Ile Val Ala Asn Val -20	271
CAC TTC AGT CAA ACT TGG GTG TTC AGT GGT AAA CCA TAT AAA GGG His Phe Ser Gln Thr Trp Val Phe Ser Gly Lys Pro Tyr Lys Gly -5 1 5 10	31.6
(2) INFORMATION FOR SEQ ID NO: 93:  (i) SEQUENCE CHARACTERISTICS:  (A) LENGTH: 405 base pairs  (B) TYPE: NUCLEIC ACID  (C) STRANDEDNESS: DOUBLE  (D) TOPOLOGY: LINEAR  (ii) MOLECULE TYPE: CDNA  (vi) ORIGINAL SOURCE:  (A) ORGANISM: Homo Sapiens  (F) TISSUE TYPE: Brain  (ix) FEATURE:  (A) NAME/KEY: sig_peptide  (B) LOCATION: 247309  (C) IDENTIFICATION METHOD: Von Heijne matrix  (D) OTHER INFORMATION: score 5.5  seq LTGLCXCCLQALG/LA  (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 93:	
ATTGTCTTAG TCCCATCCTC TGTTCCCCTG GCCAGTTTGT CTAGCTGTGT GGTCTCTGTT	60
CTCTCCCTAC CGTGCCTTCC ATCCCAGCCA TCCCTGACTA CGTGTTTCCC CCACAGACAT	120
CACACTGGTT CACCTCGTTG ACCACCGTTT CCTTCTCCCC AAGTCTCCCG GGCAAGGGCT	180
GATTCTCCAG TCTCCTCTGG GAAGCTGGCC CTGAACCACT TAGAACCTAT CGCTCCTTCG	240
TCACCT ATG TCA TGT GGC AGC GCT GCC TCA CTT ACG GGT CTG TGT KSG  Met Ser Cys Gly Ser Ala Ala Ser Leu Thr Gly Leu Cys Xaa  -20 -15 -10	288
TGC TGC CTC CAA GCC CTG GGG CTT GCG TGG CGC CGT CGC GGT TTG ACG Cys Cys Leu Gln Ala Leu Gly Leu Ala Trp Arg Arg Gly Leu Thr -5 1 5	336
GGA CCG GGC CTC CCC CCT GTG TTG CAG ATA TGC TGT CCA AGG AGC CTC Gly Pro Gly Leu Pro Pro Val Leu Gln Ile Cys Cys Pro Arg Ser Leu	384

WO 99/06552				PCT/ID08/01434
10	15	73	20	PCT/IB98/01236
CGT GGT GTG F Arg Gly Val T	ACG GCT CCT ACT Thr Ala Pro Thr 30		20	25 405
(2) INFORMATI	ON FOR SEQ ID	NO: 94:		
() ()	UENCE CHARACTE A) LENGTH: 302 B) TYPE: NUCLE C) STRANDEDNES D) TOPOLOGY: LI	base pairs CC ACID S: DOUBLE		
(ii) MOI	LECULE TYPE: CI	DNA		
( F	IGINAL SOURCE: A) ORGANISM: Ho T) TISSUE TYPE:	mo Sapiens Brain		
(D (C	ATURE:  A) NAME/KEY: si  B) LOCATION: 99  C) IDENTIFICATI  C) OTHER INFORM  UENCE DESCRIPT	236 ON METHOD: Von ATION: score seq VL	5.4 FFVGLITNGLA/MR	
AAAAATACCA GAT	GCCACTC TGCAGG	CTGC AATAACTAC	T ACTTACTGGA TACATT	
CCCTCCAGAA TCA	ACAGTTA TCAGGT	AACC AACAACIA	ATG CAA GCC GTC GAC	CAAA 60
			Met Gln Ala Val Asp -45	Asn
<b>-40</b>	-35	-3	•	ys 25
	-20	-15	F GTC CTG TTT TTT G r Val Leu Phe Phe V -10	al
-5	5	1	TITC TTT CAA ATC C Phe Phe Gln Ile A 5	GG 260 rg
AGT AAA TCA AAC Ser Lys Ser Asr 10	TTT ATT ATT TO Phe Ile Ile F	TT CTT AAG AAC he Leu Lys Asr	C ACA GTS AAG Thr Val Lys 20	302
(2) INFORMATION	FOR SEQ ID NO	: 95:		

(1) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 99 base pairs
(B) TYPE: NUCLEIC ACID

WO 99/06552		74		PC1/1	B98/U
	) STRANDEDNESS: DOUBL ) TOPOLOGY: LINEAR	E			
(ii) MOL	ECULE TYPE: CDNA				
(A	GINAL SOURCE: ) ORGANISM: Homo Sapi ) TISSUE TYPE: Brain	ens			
(B (C	TURE: ) NAME/KEY: sig_pepti ) LOCATION: 1675 ) IDENTIFICATION METH ) OTHER INFORMATION:	OD: Von He score 5.3			
(xi) SEQ	UENCE DESCRIPTION: SE	Q ID NO:	95:		
AGAAGTAGCC GCA	AGG ATG GCG GCG GCT AT Met Ala Ala Ala Me -20	G CSS TTG t Xaa Leu -15	CTC TGC TC Leu Cys Se	G TCC TGT r Ser Cys -10	51
Cys Ser Trp Gl	GC CCG GCG GCT GGT GCC Y Pro Ala Ala Gly Ala -5	Leu Gln	AAC CCC CAA Asn Pro Gln 5	CGC GGG Arg Gly	99
(2) INFORMATIO	ON FOR SEQ ID NO: 96:				
(A (B (C	JENCE CHARACTERISTICS:  A) LENGTH: 485 base pa B) TYPE: NUCLEIC ACID B) STRANDEDNESS: DOUBL B) TOPOLOGY: LINEAR	irs			
(ii) MOI	LECULE TYPE: CDNA				
(P	GÎNAL SOURCE: A) ORGANISM: Homo Sapi F) TISSUE TYPE: Brain				
(E	ATURE:  A) NAME/KEY: sig_pepti B) LOCATION: 396470 C) IDENTIFICATION METH D) OTHER INFORMATION:	IOD: Von H score 5.			
(xi) SE	QUENCE DESCRIPTION: SI	EQ ID NO:	96:		
ATTTCTGCCC AC	GGGCATAA GTTCAAAAGA A	AGCTGCGAA	AAGTTGGAGA	CTGCTGATGA	60
AACCAGTCAT CT	CCAGCCAC TCAACAAGCG TO	CAGAGGACA	AGCTCTGTGG	TGGAAGAGCA	120
TTTCCAAGCC TC	AGTATOTO COACTGAAGO O	GCACCCCCT	GCCACAGGAG	ACCAGAGTCC	180

TGGCCTGGGC ACCCAGCCAA AGCTGCCATC CAGCAGTGGC CTTCCTGCTG CAGACGTGTC 240

WO 99/06552					D	CT/IB98/01236
CCCTGCCACA GCTGAAGA	GC CCTTGTG	VCC TUTCO	75	_		
CCGAGGGCGA CTCCGCCTC	C TOTOCHUR	100 1100	ACACCC A	CCGCCGG	C CTCCCTTCA	C 300
CCGAGGGCGA CTCCGGCTC	se rerectif	'CG ATCC.	ATGGAG GA	AGGCCAGA	C TGGTGCCCA	C 360
AGTGAAAGAS CAAATACCO			Met Asp -25	Phe Ile	≥ Lys Asp -20	413
CAG TCG CTC TCG CAC Gln Ser Leu Ser His -15	AGG AGT GT Arg Ser Va	T GTG AA 1 Val Ly -1	s val Le	T TCC CT	CG AGG AAA eu Arg Lys	461
GCC CAG GCC CAG AGC Ala Gln Ala Gln Ser 1	Ile Leu Gl	A u 5				485
(2) INFORMATION FOR	SEQ ID NO:	97:				
(B) TYPE: (C) STRAN	HARACTERIST TH: 283 bas : NUCLEIC A NDEDNESS: D LOGY: LINEA	e pairs CID OUBLE				
(ii) MOLECULE T	TYPE: CDNA					
(vi) ORIGINAL S (A) ORGAN (F) TISSU	SOURCE: IISM: Homo E TYPE: Br	Sapiens ain				
(C) IDENT	KEY: sig_po ION: 591 IFICATION ( INFORMATIO	42 METHOD: DN: sco	Von Heij re 5.3 RISCAFS			
(xi) SEQUENCE D	ESCRIPTION			DU2214\ K	Q	
AGTGTGTGAA GCGTACCTAR	GGCGGGAGG	C GACATG	GWGA CAG	GGGCGGY	CGWGCTGT	58
ATG ACC AGG CCC TTT TO Met Thr Arg Pro Phe TO -25	GG GCA TCC rp Ala Ser	TGC AGC Cys Ser -20	ACG TGG Thr Trp	GCA ACG Ala Thr -15	TCC AGG Ser Arg	106
ATT TCC TGC GCG TTC TG Ile Ser Cys Ala Phe Se -10	CT TTG GCT er Leu Ala -5	TCC TCT Ser Ser	ACC GCA Thr Ala	AGA CAG Arg Gln 1	ACT TCT Thr Ser	154
	10	Int Ala	15	Ser Arg	Pro Gly 20	202
CCG CGC AGG CCT TGG TG Pro Arg Arg Pro Trp Cy 25	GC TGC AGG ys Cys Arg	TAT TCA Tyr Ser 30	AAA CCT Lys Pro	TTG ACC Leu Thr		250
CCC CTC AGG ATG ATG AG	ia aca caa	666 .				

283

COD OTO AGG ATG ATG AGA AGA GAA GGC AGY KGA

Pro Val Arg Met Met Arg Arg Glu Gly Ser Xaa 40 45

(2)	INFORMATION	FOR	SEQ	ΙD	NO:	98:

( i \	SECUENCE	CHARACTERISTICS	٠.

- (A) LENGTH: 390 base pairs
- (B) TYPE: NUCLEIC ACID
- (C) STRANDEDNESS: DOUBLE
- (D) TOPOLOGY: LINEAR
- (ii) MOLECULE TYPE: CDNA
- (vi) ORIGINAL SOURCE:
  - (A) ORGANISM: Homo Sapiens
  - (F) TISSUE TYPE: Brain
- (ix) FEATURE:
  - (A) NAME/KEY: sig\_peptide
  - (B) LOCATION: 286..333
  - (C) IDENTIFICATION METHOD: Von Heijne matrix
  - (D) OTHER INFORMATION: score 5.3

seq CAVSLTTAAVAFG/DE

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 98:

ACTNTGTGCT GGTGCTGGCA AAGTTTGTGA TTTTAAGAAA TTCTGCTGTG CTCTCCAGCA 60

CTGCGAGCTT CTGCCTTCCC TGTAGTTTCC CAGATGTGAT CCAGGTAGCC GAGATTCCGC 120

TGCCCGTGCT TCGGTAGCTT AAGTCTTTGC CTCAGCTTTT TTCCTTGCAG CCGCTGAGGA 180

GGCGATAAAA TTGGCGTCAC AGTCTCAAGC AGCGATTGAA GGCGTCTTTT CAACTACTCG 240

ATTAAGGTTG GGTATCGTCG TGGGACTTGG AAATTTGTTG TTTCC ATG AAA TCC TGC 297

Met Lys Ser Cys
-15

GCA GTG TCG CTC ACT ACC GCC GCT GTT GCC TTC GGT GAT GAG GCA AAG

Ala Val Ser Leu Thr Thr Ala Ala Val Ala Phe Gly Asp Glu Ala Lys

-10

-5

AAA ATG GCG GAA GGA AAA GCG AGC CGC GAG AGT GAA GAG GAG ACG
Lys Met Ala Glu Gly Lys Ala Ser Arg Glu Ser Glu Glu Glu Thr
5 10 15

## (2) INFORMATION FOR SEQ ID NO: 99:

- (i) SEQUENCE CHARACTERISTICS:
  - (A) LENGTH: 254 base pairs
  - (B) TYPE: NUCLEIC ACID
  - (C) STRANDEDNESS: DOUBLE
  - (D) TOPOLOGY: LINEAR
- (ii) MOLECULE TYPE: CDNA

	//	I C I/ID/0
(∨	(i) ORIGINAL SOURCE: (A) ORGANISM: Homo Sapiens (F) TISSUE TYPE: Brain	
(i	x) FEATURE:  (A) NAME/KEY: sig_peptide  (B) LOCATION: 138200  (C) IDENTIFICATION METHOD: Von Heijne matrix  (D) OTHER INFORMATION: score 5.2  seq LSLSLICLRMSLS/LY	
(x;	i) SEQUENCE DESCRIPTION: SEQ ID NO: 99:	
ATGTGATT	♥T KTTCCTATTT ATTTTAAATA CACACACCCA CAGGGCTCTG CCCCTGTA	AA 60
AGAAAAA	NA TCAAAACAAA CAAATAAATA ACCCCAAAGA GATGGACCCA GGGGAGAA	CG 120
CGTAAGTRI	CG AAGGGGC ATG AGT ATA CAC GAG TGT GCG TGT CTT TCC CTC  Met Ser Ile His Glu Cys Ala Cys Leu Ser Leu  -20 -15	170
-10	TT TGT CTC CGT ATG AGT CTC TCC TTG TAC CCT CCC CCT GCC le Cys Leu Arg Met Ser Leu Ser Leu Tyr Pro Pro Pro Ala	218
TCG ATG A Ser Met İ	TA TTA CTC CCC CAG ACT TGG AAG CCG CGC le Leu Leu Pro Gln Thr Trp Lys Pro Arg 10	254
	MATION FOR SEQ ID NO: 100:  SEQUENCE CHARACTERISTICS:  (A) LENGTH: 303 base pairs  (B) TYPE: NUCLEIC ACID  (C) STRANDEDNESS: DOUBLE  (D) TOPOLOGY: LINEAR	
(ii)	MOLECULE TYPE: CDNA	
(vi)	ORIGINAL SOURCE: (A) ORGANISM: Homo Sapiens (F) TISSUE TYPE: Brain	
(ix)	FEATURE:  (A) NAME/KEY: sig_peptide  (B) LOCATION: 178222  (C) IDENTIFICATION METHOD: Von Heijne matrix  (D) OTHER INFORMATION: score 5.2  seq SGLSFLSVFSLWC/EP	
(xi)	SEQUENCE DESCRIPTION: SEQ ID NO: 100:	
AAGATCTRGA	ARCAGTRACC CTCTCTTTT GCATRAGTTT CTCTTTTTTC TCTGAGTTAC	60
AGTTTTGARR	RCAGCWRCTA ATTTTTTTAA TCCCTCGAAT AACTCAGTTT TAGGAACATT	120
CGSTSTCCCT	AAGCCTTACC TTGAAACCAG TGTAGGATTT TGCTGCCACC CCGGAAG	177

ATG ( Met I -15	CTG . Leu	AGT Ser	GGA Gly	CTC Leu	AGC Ser	TTÇ Phe	CTA Leu	TCC Ser	GTT Val	TTC Phe -5	TCC Ser	CTC Leu	TGG Trp	TGT Cys	GAG Glu 1	225
CCC Pro	ACA Thr	CTC Leu	CCG Pro 5	GCG Ala	CTG Leu	GGA Gly	AAT Asn	GGC Gly 10	TCT Ser	GTT Val	CTA Leu	GGA Gly	GTG Val 15	CGG Arg	CWR Xaa	273
TCA :																303
(2)		) SE	QUEN	FOR CE C	HARA	.CTER	ISTI	CS:	rs							٠
			(B) (C)	TYPE STRA TOPO	: NU NDED	CLEI NESS	C AC	ID UBLE							.•	
	(i	i) M	OLEC	ULE	TYPE	: CE	NA									
	(v	i) O	(A)	NAL ORGA TISS	NISM	: Ho		_	ens							
	(i	ж) F	(A) (B) (C)	NAME LOCA	TION TIFI	: 12 CATI	03	374 SETHO	D: V	on H e 5. LYSI	2					
	( x	i) S	EQUE	NCE	DESC	RIPT	NOI?	: SE(	Q ID	NO:	101:					
AACT	TTGA	TG G	SAATO	CAAAC	GG TO	CATG	GGCGG	C CA	GGGC.	AGCT	GTT	CCCAC	CAT (	GCAG	GTGGGG	<b>60</b> ,
GCCC	GCCC	TT T	CTTO	CACA	CC TA	ACAT'	TCAA	G GA	ATTC	TGTT	GGG	CTCAT	'AA	TTCG	rtgtg	119
ATG Met -85	GGG Gly	TTA Leu	AAG Lys	GAC Asp	AAA Lys -80	TCT Ser	CAG Gln	GCC Ala	CCC Pro	GCC Ala -75	TCA Ser	GGA Gly	CTG Leu	GGA Gly	GTT Val -70	167
CTC Leu	CGA Arg	GG G	CAA Gln	AGG Arg -65	TCG Ser	GGC Gly	TCA Ser	TTC Phe	ATT Ile -60	TCT Ser	ATG Met	CCT Pro	GCC Ala	CCA Pro -55	GCC Ala	215
TCA Ser	GGC Gly	CAG Gln	TKC Xaa -50	CCG Pro	GAA Glu	GAA Glu	AGC Ser	AGG Arg -45	Ser	CCA Pro	GCT Ala	CCA Pro	CCA Pro -40	Val	GCT Ala	263
TCT Ser	AGG Arg	TCT Ser -35	CAG Gln	AAC Asn	AGA Arg	GGC Gly	TAC Tyr	Arg	CCG Pro	TGG Trp	CAT His	GGG Gly -25	CCC	CTT Leu	TGG Trp	311
															CCT	359

WO 99/0	6552			
-20		79		PCT/IB98/01236
	-15		-10	
TTT TGG G Phe Trp V -5	TT CAC GGC CGA YAG al His Gly Arg Xaa 1			380
(2) INFOR	MATION FOR SEQ ID NO:	102:		
(i)	SEQUENCE CHARACTERIS  (A) LENGTH: 265 ba  (B) TYPE: NUCLEIC  (C) STRANDEDNESS:  (D) TOPOLOGY: LINE	se pairs ACID DOUBLE		
(ii)	MOLECULE TYPE: CDNA			
(vi)	ORIGINAL SOURCE: (A) ORGANISM: Homo (F) TISSUE TYPE: B)	Sapiens cain		
(ix)	FEATURE:  (A) NAME/KEY: sig_r (B) LOCATION: 651 (C) IDENTIFICATION (D) OTHER INFORMATION	.93 METHOD: Von ON: score	Heijne matrix 5.2 QLLQVLSDVLA/EI	
(xi)	SEQUENCE DESCRIPTION			
AATT ATC AC	TTAAGGATTT TTTTTCTA	T TTTTACTCT	T TAGTTAAAAT TATA	AGACCT 60
	T GAT CAA ATT AAA TT r Asp Gln Ile Lys Ph -40	-35	sp Ser Leu Asn Ly -3	s Glu O
	AAG AAC TAT AAT TTA Lys Asn Tyr Asn Leu -25	-20	e Asp Ser Leu Glu -15	Pro
-10		b var ref	Ala Glu Ile Asp	Pro
AAG GTA AGA Lys Val Arg 5 TCT CCC TCT	GTT TTC TCT TTC TTT Val Phe Ser Phe Phe 10	TTG ATG GGT Leu Met Gly 15	Ser Arg Lys Pro	ATT 253 Ile 20
Ser Pro Ser	Trp			265

(2) INFORMATION FOR SEQ ID NO: 103:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 354 base pairs
(B) TYPE: NUCLEIC ACID
(C) STRANDEDNESS: DOUBLE

			(D) -	TOPO	LOGY	: LI	NEAF	₹								
	(i	i) 1	OLEC	ULE	TYPE	: C	ANG									
	( v	'i) (			NISM	: Ho		Sapie ain	ns							
			(B) (C)	NAME LOCA IDEN OTHE	TION TIFI R IN	: 25 CATI	ON N	METHO ON:	D: V scor seq	e 5. SSVA	1 ASLT <i>P</i>	TPSL				•
	(,,	,	LQUE	NCE	DE3C	,KIF1	LON	. SEC	, 10	NO:	103:					
AAAC	CTTG	STA (	CAACA	CCGC	sc co					Ser (					SAC Asp	51
CTG Leu -95	TGG Trp	TCA Ser	ATG Met	TGT Cys	CTG Leu -90	GAG Glu	GTC Val	CCC Pro	TCC Ser	TTT Phe -85	ACA Thr	GCC Ala	ACC Thr	GAC Asp	TCA Ser -80	99
GTG Val	AAC Asn	TGC Cys	GGC Gly	TGC Cys -75	TGT Cys	TTG Leu	GAG Glu	CTC Leu	GCG Ala -70	ACG Thr	GAG Glu	CCG Pro	GCT Ala	CGG Arg -65	AAC Asn	147
ATC Ile	AGA Arg	TCA Ser	ACC Thr -60	ACC Thr	AGG Arg	GCT Ala	TCT Ser	CTG Leu -55	CTG Leu	AGG Arg	TGC Cys	AGC Ser	TCA Ser -50	TTC Phe	ACT Thr	195
TCA Ser	ACC Thr	AGG Arg -45	AAC Asn	TCT Ser	ACG Thr	GGA Gly	ATT Ile -40	TCA Ser	GCG Ala	CTG Leu	CCT Pro	CCC Pro -35	GCG Ala	GCC Ala	CCA Pro	243
ATG Met	GCC Ala -30	TGG Trp	CCA Pro	TTC Phe	TCA Ser	GCC Ala -25	TCT Ser	TTG Leu	TCA Ser	ACG Thr	TTG Leu -20	CCA Pro	GTA Val	CCT Pro	CTA Leu	291
ACC Thr -15	CAT His	TCC Ser	TCA Ser	GTC Val	GCC Ala -10	TCC Ser	TTA Leu	ACC Thr	GCG Ala	ACA Thr	CCA Pro	TCA Ser	CTC Leu	GCA Ala	TCT Ser 1	339
			ATG Met 5													354
(2)	INF	orma	ncit.	FOR	SEQ	ID	NO:	104:								
	(:	i) S	EQUE						ł							
			(B) (C)	TYP	E: N	UCLE DNES	IC A S: D	OUBL						٠		

(ii) MOLECULE TYPE: CDNA

<pre>(vi) ORIGINAL SOURCE:     (A) ORGANISM: Homo Sapiens     (F) TISSUE TYPE: Brain</pre>	
<pre>(ix) FEATURE:     (A) NAME/KEY: sig_peptide     (B) LOCATION: 155202     (C) IDENTIFICATION METHOD: Von Heijne matrix     (D) OTHER INFORMATION: score 5.1</pre>	
(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 104:	
AACTCTGGAA TGAAGGGGGG AATTACGGGT TGGTGGTCGG CTTCATGTTA GGAGGACACC	60
CCTCCATCTG TTCACAGCTC AGCCTGTTTC CAATTTAAAG CCCAGAAGAA GCCTTCCCAG	
CCTACTCAGA ATCCCACATC CTCTCCTCTC TCTT ATG GAT CTC AGT TTT CAT TTA  Met Asp Leu Ser Phe His Leu  -15 -10	120 175
TTA CTA GAT CCT TCC TCT ACT CAA TCA AGC ATA CTG AAG CAC CTC CCA Leu Leu Asp Pro Ser Ser Thr Gln Ser Ser Ile Leu Lys His Leu Pro -5	223
TGT Cys	226
(2) INFORMATION FOR SEQ ID NO: 105:  (i) SEQUENCE CHARACTERISTICS:  (A) LENGTH: 447 base pairs (B) TYPE: NUCLEIC ACID (C) STRANDEDNESS: DOUBLE (D) TOPOLOGY: LINEAR  (ii) MOLECULE TYPE: CDNA  (vi) ORIGINAL SOURCE: (A) ORGANISM: Homo Sapiens (F) TISSUE TYPE: Brain  (ix) FEATURE: (A) NAME/KEY: sig_peptide (B) LOCATION: 289366 (C) IDENTIFICATION METHOD: Von Heijne matrix (D) OTHER INFORMATION: score 5 seq VISVLILVGFGAC/IY	
(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 105:	
ATCTCTGATG GGCAGGGAGA GATACCAGGG TGCTGAGCCA GTCCAGGACT GCCCCCTCCT	60
GGCCCACTCA GAGCCCCTGG GTGTGAGAAG CTCGTCTCCC GTGGGTTGCA TTGGCTCTGC	120
CCTATCTCTG CCTCCAGCAC CCAGGGCGGC CGCAGATGGC ACCTCTCTG GGGLGGGCGGC	130

CTGCGAATGA GTCCACGGGC CAACGCTGAG CTGCTCAGGC TGAGGCGGTG TGCTCAGCAC	240
AGAGCCCCCG GAACTGGCAT CTGCAGGGCG TGAGCCAARG CCGCCGCG ATG CCG CAC  Met Pro His  -25	297
TTC CTG GAC TGG TTC GTG MCG GTC TAC TTG GTC ATC TCG GTC CTC ATT Phe Leu Asp Trp Phe Val Xaa Val Tyr Leu Val Ile Ser Val Leu Ile -20 -15 -10	345
CTG GTG GGC TTC GGC GCC TGC ATC TAC TTC GAG CCG GGC CTG CAG Leu Val Gly Phe Gly Ala Cys Ile Tyr Tyr Phe Glu Pro Gly Leu Gln -5 1 5	393
GAG GCG CAC AAG TGG CGC ATG YAG CGC CCC TGG TGG ACC GCG ACC TCC Glu Ala His Lys Trp Arg Met Xaa Arg Pro Trp Trp Thr Ala Thr Ser 10 20 25	441
ACT GGG Thr Gly	447
(2) INFORMATION FOR SEQ ID NO: 106:  (i) SEQUENCE CHARACTERISTICS:  (A) LENGTH: 195 base pairs  (B) TYPE: NUCLEIC ACID  (C) STRANDEDNESS: DOUBLE  (D) TOPOLOGY: LINEAR  (ii) MOLECULE TYPE: CDNA  (vi) ORIGINAL SOURCE:  (A) ORGANISM: Homo Sapiens  (F) TISSUE TYPE: Brain  (ix) FEATURE:  (A) NAME/KEY: sig_peptide  (B) LOCATION: 79168  (C) IDENTIFICATION METHOD: Von Heijne matrix  (D) OTHER INFORMATION: score 5  seq IVGLLAQLEKINA/EP  (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 106:	
AACAGAAAGA TGACTTAAAG AACGTGGGGA GTCGCTCGCA GTTCGATTAT CTGCAATTAT	60
GAAATGAAGT AACTCAAG ATG AGC AAG TTA AAA GTG ATA CCA GAA AAA AGC Met Ser Lys Leu Lys Val Ile Pro Glu Lys Ser -30 -25 -20	111
CTT ACC AAT AAT TCT AGG ATC GTA GGA CTC CTG GCT CAA CTG GAG AAG Leu Thr Asn Asn Ser Arg Ile Val Gly Leu Leu Ala Gln Leu Glu Lys -15 -10 -5	159
ATC AAT GCT GAG CCT TCA GAA TCW GAC ACT AGC CGG Ile Asn Ala Glu Pro Ser Glu Ser Asp Thr Ser Arg 1 5	195

(2) INFORMATION FOR SEQ ID NO: 107:	
(i) SEQUENCE CHARACTERISTICS:  (A) LENGTH: 166 base pairs  (B) TYPE: NUCLEIC ACID  (C) STRANDEDNESS: DOUBLE  (D) TOPOLOGY: LINEAR	
(ii) MOLECULE TYPE: CDNA	
<pre>(vi) ORIGINAL SOURCE:     (A) ORGANISM: Homo Sapiens     (F) TISSUE TYPE: Brain</pre>	
<pre>(ix) FEATURE:     (A) NAME/KEY: sig_peptide     (B) LOCATION: 38106     (C) IDENTIFICATION METHOD: Von Heijne matrix     (D) OTHER INFORMATION: score 5</pre>	•
(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 107:	
AACTGCTGCT CACAGAAGCA GTGAGGATGA TGCCAGG ATG ATG TCT GCC TCG CGC Met Met Ser Ala Ser Arg -20	55
CTG GCT GGG ACT CTG ATC CCA GCC ATG GCC TTC CTC TCC TGC GTG AGA Leu Ala Gly Thr Leu Ile Pro Ala Met Ala Phe Leu Ser Cys Val Arg -15 -10 -5	103
CCA GAA AGC WGG GAG CCC TGC GTG GAG GTG GTT CCT AAT ATT ACT TAT Pro Glu Ser Xaa Glu Pro Cys Val Glu Val Val Pro Asn Ile Thr Tyr  1 5 10 15	151
CAA TGC ATG GAG CTG Gln Cys Met Glu Leu 20	166
(2) INFORMATION FOR SEQ ID NO: 108:	
(i) SEQUENCE CHARACTERISTICS:  (A) LENGTH: 278 base pairs  (B) TYPE: NUCLEIC ACID  (C) STRANDEDNESS: DOUBLE  (D) TOPOLOGY: LINEAR	
(11) MOLECULE TYPE: CDNA	
<pre>(v1) ORIGINAL SOURCE:   (A) ORGANISM: Homo Sapiens   (F) TISSUE TYPE: Brain</pre>	

(ix) FEATURE:

(A) NAME/KEY: sig\_peptide

(B) LOCATION: 84230 (C) IDENTIFICATION METHOD: Von Heijne matrix (D) OTHER INFORMATION: score 4.9 seq VTVCCXLVAFLFC/IL	
(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 108:	
AARAGACTCC GCCCCCTTCC TTGGAGCGCC GCGNCTCGGG CTGAGGGAGC TCGGGCCAAT	60
CAGAGGGACG GCCCCAGART GGC ATG GTA GAT GGA ACG CAG CTG AGA GGT CTG  Met Val Asp Gly Thr Gln Leu Arg Gly Leu  -45	113
ACA AGA ATG TAC CAG GTC CCA CTA MCA CTG GAT CGG GAT GAG ACC CTG Thr Arg Met Tyr Gln Val Pro Leu Xaa Leu Asp Arg Asp Glu Thr Leu -35 -30 -25	161
GTA CGG CTC CGC TTC ACC ATG GTG GCC CTG GTC ACG GTC TGC TGT MCA Val Arg Leu Arg Phe Thr Met Val Ala Leu Val Thr Val Cys Cys Xaa20 -15 -10	209
CTT GTC GCC TTC CTC TTC TGC ATC CTC TGG TCC CTG CTC TTC CAC TTC Leu Val Ala Phe Leu Phe Cys Ile Leu Trp Ser Leu Leu Phe His Phe -5	257
AAG GAG ACA ACG GCC ACA GGG Lys Glu Thr Thr Ala Thr Gly 10 15	278
(2) INFORMATION FOR SEQ ID NO: 109:  (i) SEQUENCE CHARACTERISTICS:  (A) LENGTH: 217 base pairs  (B) TYPE: NUCLEIC ACID  (C) STRANDEDNESS: DOUBLE  (D) TOPOLOGY: LINEAR  (ii) MOLECULE TYPE: CDNA  (vi) ORIGINAL SOURCE:  (A) ORGANISM: Homo Sapiens	
(F) TISSUE TYPE: Brain  (ix) FEATURE:  (A) NAME/KEY: sig_peptide  (B) LOCATION: 116193  (C) IDENTIFICATION METHOD: Von Heijne matrix  (D) OTHER INFORMATION: score 4.9  seq LISMLQMLAVIIT/NT	
(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 109:	
ACTIGAAGIT CYYCIGGGG CAAIGAGAIG GCAGCIATAC AGCGAGICIG AAAAGAACAI	6
CCACATTCCT AATCCCTAGG AATATGATTA TTGGAAAATA GATATAATTA TACAA ATG Met	11

Lys -25	CAG Glu	AAC Asn	TTC Phe	CTT Leu	GTT Val -20	CTC . Leu	AAC Asn	AGT ( Ser	GTC Val	TGG Trp -15	TAC Tyr	CTA Leu	ATA Ile	AGC Ser	ATG Met -10	166
	CAA Gln															214
GGG Gly																217
(2)	INFO	RMAT	ION	FOR	SEQ	ID N	0: 1	10:								
	(i	) SE	(A) (B) (C)	LENG TYPE STRA	HARA TH: : NU NDED LOGY	426 CLEI NESS	base C AC : DO	pai ID UBLE								
	(i	i) M	OLEC	ULE	TYPE	: CD	AN									
	( v	i) O	(A)	ORGA	SOUR MISM SUE T	: Но		-	ns							
	( i	×) F	(A) (B) (C)	NAME LOCA IDEN	TIFI TION	: 55 CATI	23 ON M	1 ETHO		Jon H	leijr	ne ma	atri	ς.		
			(D)	OTHE	ER IN	IFORM	ATIC			te 4.		LGS:	SA/GI	)		
	( )	(i) S			DESC				seq	LVEM	CLE		SA/GI	)		
аат:	() TCAGA		EQUE	ENCE	DESC	CRIPI	`ION:	SEÇ	seq D ID	NO:	110	:			ATG Met	57
GAA	rcage	AAT T	EQUE TAGA! AAT	ence Aaac agt	DESC AA AC TCT	CRIPT CCAGI	'ION': TAGAT	SEÇ TTTT AAG	seq ) ID TTTT	LVEM NO: GAAC TTA	110 AAA CTA	: AATC GTT	TTT GAA	AGAA AAG	Met TCA	57 105
GAA Glu CTT	TGT Cys GTG	CAA Gln AAA	FAGAZ AAT Asn -55 GCT	AAAC. AGT Ser TCT	DESC AA AC TCT Ser TAT	CRIPT CCAGI TTA Leu TTA	TAGAT AAA Lys ATT	SEC TTTT AAG Lys -50 GCT	seq () ID (TTT) TGT Cys	LVEM NO: GAAC TTA Leu CAA	AAA CTA Leu	: AATC GTT Val GCT	GAA Glu -45 GCA Ala	AGAA AAG Lys AGC	Met TCA	
GAA Glu CTT Leu	TGT Cys GTG Val	CAA Gln AAA Lys -40	AAT Asn -55 GCT Ala	AAACA AGT Ser TCT Ser	DESC AA AC TCT Ser TAT Tyr	CCAGI TTA Leu TTA Leu GAA	TAGAT  AAA  Lys  ATT  Ile  -35	SECT TTTT  AAG Lys -50 GCT Ala TTA	seq ID TTTT Cys TTC Phe	NO: GAAC TTA Leu CAA Gln	AAA CTA Leu ACT Thr	GTT Val GCT Ala -30 TAT	TTT  GAA Glu -45 GCA Ala	AGAA AAG Lys AGC Ser	Met TCA Ser	105
GAA Glu CTT Leu AAG Lys	TGT Cys GTG Val CCA Pro -25 TGT Cys	CAA Gln AAA Lys -40 TTC Phe	AAT Asn -55 GCT Ala TCB Ser	AAAC. AGT TCT Ser ATT Ile	DESC AA AG TOT Ser TAT Tyr GGT Ala	TTA Leu  TTA Leu  GAA Glu -20  GGT Gly	AAA Lys ATT Ile -35 GAA Glu	SECT TTTT  AAG Lys -50 GCT Ala  TTA Leu  AGT	seq ) ID TTTTO TGT Cys TTC Phe ATT Ile	NO: GAAC TTA Leu CAA Gln AAA Lys	AAAA CTA Leu ACT Thr CCA Pro-15	GTT Val GCT Ala -30 TAT Tyr	GAA Glu -45 GCA Ala TTA	AAGAA AAGC Lys AGC Ser Val	Met TCA Ser AAG Lys GAA Glu ACT Thr	105
GAA Glu CTT Leu AAG Lys ATG Met -10	TGT Cys GTG Val CCA Pro -25 TGT Cys	CAA Gln AAA Lys -40 TTC Phe TTA Leu	AAT ASN -55 GCT Ala TCB Ser GAA Glu	AGTT Val	DESC AA AC TCT Ser TAT Tyr GCT Ala TTS Leu -5	TTA Leu TTA Leu GAA Glu -20 GGT Gly	AAA Lys ATT Ile -35 GAA Glu TCA Ser	SECONT TTM  AAG Lys -50 GCT Ala TTA Leu AGT Ser	seq ) 10  TTTTC  TGT Cys  TTC Phe  ATT Ile  GGT Ala  CAC His	CAA Gln AAA Lys CGA Sly AGG	AAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAA	GTT Val GCT Alaa-30 TAT Tyr AAAA	GAA Glu -45 GCA Ala TTA Leu A ATC	AAGAAA AAGA Lys AGC Ser Val	Met TCA Ser AAG Lys GAA Glu ACT Thr	105 153 201

Ala	qsA.	Ile.	Glu	Asp	Gln	Leu	Ile	Gln	Lys	Val	Arg	Glu	Ser	Lys	Trp
		25					30					25		-	-

TTT GCC CTT CAG ATA GAT GAG TCA TCA GAA ATC TCA AAT ATC ACA CTT

Phe Ala Leu Gln Ile Asp Glu Ser Ser Glu Ile Ser Asn Ile Thr Leu

40

45

CTT TTG TGC TAT ATT CGT TTC ATT GAT TAT GAT
Leu Leu Cys Tyr Ile Arg Phe Ile Asp Tyr Asp
55 60 65

#### (2) INFORMATION FOR SEQ ID NO: 111:

- (i) SEQUENCE CHARACTERISTICS:
  - (A) LENGTH: 95 base pairs
  - (B) TYPE: NUCLEIC ACID
  - (C) STRANDEDNESS: DOUBLE
  - (D) TOPOLOGY: LINEAR
- (ii) MOLECULE TYPE: CDNA
- (vi) ORIGINAL SOURCE:
  - (A) ORGANISM: Homo Sapiens
  - (F) TISSUE TYPE: Brain
- (ix) FEATURE:
  - (A) NAME/KEY: sig\_peptide
  - (B) LOCATION: 15..83
  - (C) IDENTIFICATION METHOD: Von Heijne matrix
  - (D) OTHER INFORMATION: score 4.8

seq VMWLVALLEMCVC/KK

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 111:

ATTGAAAAAT AAAA ATG CAC TCT AGT ATA AAA ACG AAG GGA AGC GTC ATG 50

Met His Ser Ser Ile Lys Thr Lys Gly Ser Val Met
-20 -15

TGG CTT GTT GCT CTT TTG GAG ATG TGT GTG TGT AAG AAG TCC AGG

Trp Leu Val Ala Leu Leu Glu Met Cys Val Cys Lys Lys Ser Arg

-10

-5

# (2) INFORMATION FOR SEQ ID NO: 112:

- (i) SEQUENCE CHARACTERISTICS:
  - (A) LENGTH: 473 base pairs
  - (B) TYPE: NUCLEIC ACID
  - (C) STRANDEDNESS: DOUBLE
  - (D) TOPOLOGY: LINEAR
- (ii) MOLECULE TYPE: CDNA
- (vi) ORIGINAL SOURCE:
  - (A) ORGANISM: Homo Sapiens
  - (F) TISSUE TYPE: Brain

	87 PC1	/IB98/
(ix)	) FEATURE:  (A) NAME/KEY: sig_peptide  (B) LOCATION: 342395  (C) IDENTIFICATION METHOD: Von Heijne matrix  (D) OTHER INFORMATION: score 4.8	
	seq LEAISSLSSFVLG/RM	
(xi)	SEQUENCE DESCRIPTION: SEQ ID NO: 112:	
ACTGTTTATA	GATATTTTGT TTCCCTGAGC AACAGAAAAT GCAGTGCTTA TTTAACTTAG	60
CAGCAATGCC	TTGTAAAAAT ATAAGCCTGC AGATGGCAAT GGCCTCTATT TTTCTTCCAC	100
AAGTTTCTTC	CAATTCAGAG CCCGTGCCTT CCTTCAGCCA CAGAGCGCAC AACAGCATGG	120
ATGAGATTGA	GTCAGCCCTC TTACATTGTT GGCCTACAGC TATCCACCTA COTTAGE	
GTTGTCCACT	TTGGGGTTTG AGCATGGGAA GTAAATTCAG AGATGCAAGT ATCTGGGAGA	240
GGGCATCAAC	TECHNOLOGICAL GIAMATTCAG AGATGCAAGT ATCTGGGAGA	300
	Met Thr Val Leu Pro -15	356
	-10 -5 1 Leu Gly Arg Met Asn	404
AGC AGA GGG Ser Arg Gly 5	G GCA GGA AAG ACC CAG AAT CTT GAT GCC AGC TCC YTG CTT  / Ala Gly Lys Thr Gln Asn Leu Asp Ala Ser Ser Leu Leu  10 15	452
TTA CTC TGC Leu Leu Cys 20	C TGC TTG ATA CTG 5 Cys Leu Ile Leu 25	473
(2) INFORMA	TION FOR SEQ ID NO: 113:	
(i) Si	EQUENCE CHARACTERISTICS:  (A) LENGTH: 386 base pairs  (B) TYPE: NUCLEIC ACID  (C) STRANDEDNESS: DOUBLE  (D) TOPOLOGY: LINEAR	
(ii) N	MOLECULE TYPE: CDNA	
(vi) (	ORIGINAL SOURCE: (A) ORGANISM: Homo Sapiens (F) TISSUE TYPE: Brain	
(ix) F	FEATURE:  (A) NAME/KEY: sig_peptide  (B) LOCATION: 12101  (C) IDENTIFICATION METHOD: Von Heijne matrix  (D) OTHER INFORMATION: score 4.8	

seq ILFCVGAVGACTL/SV

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 113:

WO 99/06552 88 PCT/IB98/01236

AATA	CACA	AGA P	: G17			, Ser			His	CTG Leu	50
				CTA Leu							98
				CCG Pro 5							146
				TGT Cys							194
				TGG Trp							242
				TGC Cys							290
				AAC Asn							338
				ATT Ile 85							386

### (2) INFORMATION FOR SEQ ID NO: 114:

- (i) SEQUENCE CHARACTERISTICS:
  - (A) LENGTH: 147 base pairs
  - (B) TYPE: NUCLEIC ACID
  - (C) STRANDEDNESS: DOUBLE
  - (D) TOPOLOGY: LINEAR
- (ii) MOLECULE TYPE: CDNA
- (vi) ORIGINAL SOURCE:
  - (A) ORGANISM: Homo Sapiens
  - (F) TISSUE TYPE: Brain
- (ix) FEATURE:
  - (A) NAME/KEY: sig\_peptide
  - (B) LOCATION: 10..84
  - (C) IDENTIFICATION METHOD: Von Heijne matrix
  - (D) OTHER INFORMATION: score 4.8

seq ALFYSVVVSTVSG/NE

(xi) SEQUENCE DESCRIPTION: SEO ID NO: 114:

AAGAGTCTG ATG AAT AGC AGT AAA GAA GAA ATG CGC GAA CTG GCA GCG TTG 5
Met Asn Ser Ser Lys Glu Glu Met Arg Glu Leu Ala Ala Leu

WO 99/06552		89		PCT/IB98/01236	
-25		-20		15	
TTT TAT TCT GTA GTC Phe Tyr Ser Val Val -10					
ATG ATA GAA CAG CTT Met Ile Glu Gln Leu 10	lle Lys T	ACT ACA AAA Thr Thr Lys 15	GAC AAT CAC Asp Asn His	AGC CTA G Ser Leu A 20	CGG 147 Arg
(2) INFORMATION FOR	SEQ ID NO	): 115:			
(B) TYE (C) STE	CHARACTERI GTH: 297 b E: NUCLEIC ANDEDNESS: OLOGY: LIN	base pairs C ACID C DOUBLE			
(ii) MOLECULE	TYPE: CDN	AN			
	SOURCE: SANISM: Hom	•			
(B) LOC (C) IDE	ME/KEY: sig	210 ON METHOD: V ATION: sco:	Von Heijne m re 4.7 LLAKALHLLKS		
(xi) SEQUENCE	E DESCRIPT	ION: SEQ ID	NO: 115:		
AAGTTGTGCG CCGGTCC	CTG GGCCTG	AGCT CCGGCT	CCGG CTGGGGG		ATG 57 Met
TCT CAA GAT GGC GG. Ser Gln Asp Gly Gl -50					
CGG GTG TCT GAG CT Arg Val Ser Glu Le	u Gln Val	CTT CTT GGC Leu Leu Gly	Phe Ala Gl	y Arg Asn	AAG 153 Lys

-35

-30

-15

15

AGT GGA CGG AAG CAC GAG CTC CTG GCC AAG GCT CTG CAC CTC CTG AAG

Ser Gly Arg Lys His Glu Leu Leu Ala Lys Ala Leu His Leu Leu Lys

TOO AGO TGT GOO COT AGT GTO CAG ATG AAG ATG AAA GAG CTT TAC CGA

Ser Ser Cys Ala Pro Ser Val Gln Mot Lys Ile Lys Glu Leu Tyr Arg

CGA CGC TTT CCC CGG AAG ACC CTG GGG CCC TCT GAT CTC TCC TCC GGG Arg Arg Phe Pro Arg Lys Thr Leu Gly Pro Ser Asp Leu Ser Ser Gly

-10

201

249

PCT/IB98/01236 WO 99/06552 90

(2)	INFORMATION	FOR	SEO	ID	NO:	116:
-----	-------------	-----	-----	----	-----	------

- (i) SEQUENCE CHARACTERISTICS:
  - (A) LENGTH: 141 base pairs
  - (B) TYPE: NUCLEIC ACID
  - (C) STRANDEDNESS: DOUBLE
  - (D) TOPOLOGY: LINEAR
- (ii) MOLECULE TYPE: CDNA
- (vi) ORIGINAL SOURCE:
  - (A) ORGANISM: Homo Sapiens
  - (F) TISSUE TYPE: Brain
- (ix) FEATURE:
  - (A) NAME/KEY: sig\_peptide
  - (B) LOCATION: 1..87
  - (C) IDENTIFICATION METHOD: Von Heijne matrix
  - (D) OTHER INFORMATION: score 4.7

seq LCYLSIFCLGVLF/II

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 116:

ATG CCT TGT ATA TCT CTC TTA GGT CTA CTT TAT AAT TTT GTT CAA GTC 48 Met Pro Cys Ile Ser Leu Leu Gly Leu Leu Tyr Asn Phe Val Gln Val -25

CTC TGT TAC TTA TCG ATC TTC TGT CTA GGT GTT CTG TTC ATT ATT GAA 96 Leu Cys Tyr Leu Ser Ile Phe Cys Leu Gly Val Leu Phe Ile Ile Glu -10

CGT GGT TCA TTA AAA GTC TCC AAA TTA ATC TGT AGG CCA CCA GGG Arg Gly Ser Leu Lys Val Ser Lys Leu Ile Cys Arg Pro Pro Gly 10

- (2) INFORMATION FOR SEQ ID NO: 117:
  - (i) SEQUENCE CHARACTERISTICS:
    - (A) LENGTH: 307 base pairs
    - (B) TYPE: NUCLEIC ACID
    - (C) STRANDEDNESS: DOUBLE
    - (D) TOPOLOGY: LINEAR
  - (ii) MOLECULE TYPE: CDNA
  - (vi) ORIGINAL SOURCE:
    - (A) ORGANISM: Homo Sapiens
    - (F) TISSUE TYPE: Brain
  - (ix) FEATURE:
    - (A) NAME/KEY: sig\_peptide
    - (B) LOCATION: 167..211
    - (C) IDENTIFICATION METHOD: Von Heijne matrix
    - (D) OTHER INFORMATION: score 4.7

seq IAVLFCFFLLIIF/QT

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 117:

		91	1 6 1/10/0/
AACTAAGVWN KTTCAGC	AAA TACTTTTCA	A CATTCCCTTC TGTCCT	TTCT TTGTTTTTAA 60
AGAAAGCTCT GATTTTGT	TTT CATTTTCAG	C TGGAGACTTA AATGAC	ACCA AGCAAAGCCT 120
ACTTAGTTTA GATCTCCA	AGA AATTGGCTG(	3 TGGAAAAAA TCAAAC	ATG AAG ATT 175 Met Lys Ile -15
GCA GTT TTG TTT TGT Ala Val Leu Phe Cys -10	-5	Led lie lie Phe Glr	n Thr Asp Phe
GGA AAA AAT GAA GAA Gly Lys Asn Glu Glu 5	10	15 Ups Gin Arg Arg Lys	G ATC TAC CAC 27.1 F Ile Tyr His 20
AGA AGG TTG AGG AAA Arg Arg Leu Arg Lys 25	AGT TCA ACC Ser Ser Thr	TCA CAC AAG CAG Ser His Lys Gln 30	307
/2) INCORNA			

- (2) INFORMATION FOR SEQ ID NO: 118:
  - (i) SEQUENCE CHARACTERISTICS:
    - (A) LENGTH: 396 base pairs
    - (B) TYPE: NUCLEIC ACID
    - (C) STRANDEDNESS: DOUBLE
    - (D) TOPOLOGY: LINEAR
  - (ii) MOLECULE TYPE: CDNA
  - (vi) ORIGINAL SOURCE:
    - (A) ORGANISM: Homo Sapiens
    - (F) TISSUE TYPE: Brain
  - (ix) FEATURE:
    - (A) NAME/KEY: sig\_peptide
    - (B) LOCATION: 253..381
    - (C) IDENTIFICATION METHOD: Von Heijne matrix
    - (D) OTHER INFORMATION: score 4.7

seq STWSSASLRGSWQ/QG

- (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 118:
- AATACTGATG TCTYCCGAAA AACACAGCCC CAAGGGAGTC GAGACGWTGT ACCAGGTAGA
- ATAAGGCACA GGGGAGCCGC TTGACAAATC AGACGACGGC AGCCGGCCTG CCTGCCCGGT 120
- ATGTGGCCAA ATATGGGCGA GGCCAAGGTT GGGGTGTGAA AGTGCGTGAC GTTTACACCC 180
- ACGTGGGCGT CTGTGCACGT GCGTGTGTGC GTGTGAGCTG CCTGTGGGCA TCTGCAGAAG 240
- CAGACATTCT TO ATG GCT AAA CAA AAA CCT CAC GTT TTG GGT TCC AGG GTG Met Ala Lys Gln Lys Pro His Val Leu Gly Ser Arg Val
- ATG CCA GCG AGT TGT GTT TCT GAG AGA CGA AGG AAG CCT TCC TTC CAG Met Pro Ala Cer Cys Val Ser Gl: Arg Arg Arg Lys Pro Ser Phe Gln 339

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 119:

1

GAT GTA TCA TTG GGG GCA AGG

Asp Val Ser Leu Gly Ala Arg

(2) INFORMATION FOR SEQ ID NO: 120:

(ii) MOLECULE TYPE: CDNA

(vi) ORIGINAL SOURCE:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 460 base pairs
(B) TYPE: NUCLEIC ACID
(C) STRANDEDNESS: DOUBLE
(D) TOPOLOGY: LINEAR

-5

ATGGAGATCC ATAACATGAT CCTACATGAA TGTTTCAATA TTGTATTCCT GTAAGTTACT

GGTTTTGTAG AAGGTCGTAT CC ATG GGT TTT TTA TAT TTG AAA AGT GTT TTC

TTTACATTGA CAGTTCTGAA ATTCATGTTG AGTGTTAATT AGGCAGGAAA TCAGAAGGGA 120

Met Gly Phe Leu Tyr Leu Lys Ser Val Phe ~15

172

193

93	
(A) ORGANISM: Home Sapiens (F) TISSUE TYPE: Brain	
<ul> <li>(ix) FEATURE:</li> <li>(A) NAME/KEY: sig_peptide</li> <li>(B) LOCATION: 254436</li> <li>(C) IDENTIFICATION METHOD: Von Heijne matrix</li> <li>(D) OTHER INFORMATION: score 4.6</li> <li>seq LLLLHGGGHSALS/WA</li> </ul>	
(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 120:	
AAGTTTACGG AGCCGGTGGG CGGTAGGCGG TGCTACGGGT AGCTGGGTGC TGTCCAAAGG 6	50
CGACAGGGCG TCGTTAGGGG AGCGAGTCGT GACCGGTTGG GCCACACTCA ACGTGGGACG 12	20
AAGCTTCGCC TACTGTTTGA CTACGTGCGT GCAGCCTCCC CTCGATGTCG GCCCTCGAAA 18	30
AGAGCATGCA CCTCGGCCGC CTTCCCTCTC GCCCACCTCT ACCCGGCAGC GGGGGCAGTC 24	10
AGAGCGGASC AAG ATG CGA ATG GGC CCT GGA AGA AAG CGG GAC TTT TCC 28  Met Arg Met Gly Pro Gly Arg Lys Arg Asp Phe Ser  -50 -50	39
CCT GTT CCT TGG AGT CAG TAT TTT GAG TCC ATG GAA GAT GTA GAA GTA Pro Val Pro Trp Ser Gln Tyr Phe Glu Ser Met Glu Asp Val Glu Val -45 -40 -35	37
GAG AAT GAA ACT GGC AAG GAT ACT TTT CGA GTC TAC AAG AGT GGT TCA Glu Asn Glu Thr Gly Lys Asp Thr Phe Arg Val Tyr Lys Ser Gly Ser -30 -25 -20	85
GAG GGT CCA GTC CTG CTC CTG CAT GGA GGA GGT CAT TCT GCC CTT Glu Gly Pro Val Leu Leu Leu His Gly Gly Gly His Ser Ala Leu -15 -10 -5	33
TCT TGG GCT GTG TTC ACG GCA GCT ARG  Ser Trp Ala Val Phe Thr Ala Ala Xaa  1 5	60
(2) INFORMATION FOR SEQ ID NO: 121:	
(i) SEQUENCE CHARACTERISTICS:  (A) LENGTH: 275 base pairs  (B) TYPE: NUCLEIC ACID  (C) STRANDEDNESS: DOUBLE  (D) TOPOLOGY: LINEAR	
(ii) MOLECULE TYPE: CDNA	
(vi) OPIGINAL SOURCE:  Al ORGANISM: Homb Sapiens  Pl TISSUE TYPE: Brain	

(A) NAME/KEY: sig\_peptide
(B) LOCATION: 2071.245
(C) IDENTIFICATION METHOD: Von Heitne matrix

(ix) FEATURE:

700552

seq MIFLLYLLPSSEE/RR

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 121:

(D) OTHER INFORMATION: score 4.6

AAACAGACAG GTATGGAGTC TGGGTGGGGC CACGTGTACC CTCCCATCCT TAGAAAGAGT 60

GTGACACCAA GGGACAGATG CTGGCGTASG CGGGTTTTGT TTTGGAGGGT TTTTTGTTTG 120

TTTTTACAAA AATTAAGATA TTTCTGAGTT TATTATGAGG CTTTTAGTTT TACAATCATA 180

CTAAAAGATA ATTGTTCCTC TATAAA ATG ATT TTC CTT CTG TAC CTC TTG CCT 233

Met Ile Phe Leu Leu Tyr Leu Leu Pro

-10 -5

TCT TCT GAA GAA AGG AGA AAA TTG CTT TTT AGT CCC CAC AGG

Ser Ser Glu Glu Arg Arg Lys Leu Leu Phe Ser Pro His Arg

1 5 10

#### (2) INFORMATION FOR SEQ ID NO: 122:

- (i) SEQUENCE CHARACTERISTICS:
  - (A) LENGTH: 445 base pairs
  - (B) TYPE: NUCLEIC ACID
  - (C) STRANDEDNESS: DOUBLE
  - (D) TOPOLOGY: LINEAR
- (ii) MOLECULE TYPE: CDNA
- (vi) ORIGINAL SOURCE:
  - (A) ORGANISM: Homo Sapiens
  - (F) TISSUE TYPE: Brain
- (ix) FEATURE:
  - (A) NAME/KEY: sig\_peptide
  - (B) LOCATION: 236..418
  - (C) IDENTIFICATION METHOD: Von Heijne matrix
  - (D) OTHER INFORMATION: score 4.6

seg LLLLHGGGHSALS/WA

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 122:

GCGGTAGGCG GGTGCTACGG GTAGCTGGGT GCTGTCCAAA GGCGACAGGG CGTCGTTAGG 60

GGAGCGAGTC GTGACCGGTT GGGCCACACT CAACGTGGGA CGAAGCTTCG CCTACTGTTT 120

GACTACGTGC GTGCAGCCTC CCCTCGATGT CGGCCCTCGA AAAGAGCATG CACCTCGGCC 180

GCCTTCCCTC TCGCCCACCT CTACCCGGCA GCGGGGGCAG TCAGAGCGGA SCAAG ATG 238

CGA ATG GGC CCT GGA AGA AAG CGG GAC TTT TCC CCT GTT CCT TGG AGT

Arg Met Gly Pro Gly Arg Lys Arg Asp Phe Ser Pro Val Pro Trp Ser

-60

-50

-50

CAG TAT TTT GAG TCC ATG GAA GAT GTA GAA GTA GAG AAT GAA ACT GGC Gln Tyr Phe Glu Ser Met Glu Asp Val Glu Val Glu Asn Glu Thr Gly

wo	99/0655	2			PCT/	B98/01236									
			-40					-35					-30		
AAG GA Lys As	T ACT p Thr	TTT Phe -25	CGA Arg	GTC Val	TAC Tyr	AAG Lys	AGT Ser -20	GGT Gly	TCA Ser	GAG Glu	GGT Gly	CCA Pro -15	GTC Val	CTG Leu	382
CTC CT Leu Le															430
ACG GC. Thr Al															445
	(ii) SE (iii) N (vi) (	CQUEN (A) (B) (C) (D)  MOLEC (A) (F)  FEATT (A) (B) (C)	ICE C LENC TYPE STRA TOPC CULE INAL ORGA TISS JRE: NAME LOCA IDEN	CHARACTH: C: NC NDEE NLOGY TYPE SOUR NISM SUE T	ACTER 138 JCLEI DNESS 1: LI CE: CE TYPE: 1: 49 ICATI	RISTI base CC AC CINEAR DNA DMO S Bra Lg_pe 1996	ICS: Pai DUBLE Sapie ain Eptic METHO	ens de			ne m	atri:	۲.		
	(xi) :							seq	LLNI	LISII		PS/QI	7		
ATATAC	CTGAA '	TTAA	GTGT	CT C	TTGG	TAAT	A CA	GGCT	CTTA	TCA	AACC			u Ser	57
CTA TT Leu Le								Ser							105
CCA CF Pro Gl						Leu									138
(2) Iì	NFORMA	GOIT.	FOR	SEQ	ID	: OZ	124:								
	(1) S	(A) (B) (C)	LEN TYP STR	CHAR GTH: E: N ANDE OLOG	9† UCLE DNES	base IC A S: D	pai CID OUBL	rs							

(ii) MOLECULE TYPE: CDNA

<pre>(vi) ORIGINAL SOURCE:     (A) ORGANISM: Homo Sapiens     (F) TISSUE TYPE: Brain</pre>	
<pre>(ix) FEATURE:     (A) NAME/KEY: sig_peptide     (B) LOCATION: 1185     (C) IDENTIFICATION METHOD: Von Heijne matrix     (D) OTHER INFORMATION: score 4.5</pre>	
(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 124:	•
AAGATTCATC ATG GGC ACC ACC TCC AAC ATG GTC ACC ACC ATC CAT CTC Met Gly Thr Thr Ser Asn Met Val Thr Thr Ile His Leu -25 -20 -15	49
ATG TTG CTG TGG CCA GTG CAT CCA TTA CTG GTG GGC CAC CGC GGG Met Leu Trp Pro Val His Pro Leu Leu Val Gly His Arg Gly -10 -5 1	94
(2) INFORMATION FOR SEQ ID NO: 125:  (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 481 base pairs (B) TYPE: NUCLEIC ACID (C) STRANDEDNESS: DOUBLE (D) TOPOLOGY: LINEAR  (ii) MOLECULE TYPE: CDNA  (vi) ORIGINAL SOURCE: (A) ORGANISM: Homo Sapiens (F) TISSUE TYPE: Brain  (ix) FEATURE: (A) NAME/KEY: sig_peptide (B) LOCATION: 41343 (C) IDENTIFICATION METHOD: Von Heijne matrix	
(D) OTHER INFORMATION: score 4.4 seq ISHILAFFAASDG/IV	
(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 125:	
AAGTTCCCTC AGCGCCCGTA GCTTCGGCGG AGTCTGCGCG ATG GGC GAC CCG GAA Met Gly Asp Pro Glu -100	55
AGG CCG GAA GCG GCC GGG CTG GAT CAG GAT GAG AGA TCA TCT TCA GAC Arg Pro Glu Ala Ala Gly Leu Asp Gln Asp Glu Arg Ser Ser Ser Asp -95 -85	103
ACC AAC GAA AGT GAA ATA AAG TCA AAT GAA GAG CCA CTC CTA AGA AAG Thr Ash Glu Ser Glu Ile Lys Ser Ash Glu Glu Pro Leu Leu Arg Lys	151

										9/					_	
-80					-75					70	)				-65	
		,		<b>-</b> 60			rne	Pro	-55	GIn	Tyr	Pro	Asp	-50		199
		-	-45	0111	1114	GIN	мта	-40	Phe	Trp	Thr	Ala	Glu -35	Glu		247
GAC Asp	TTA Leu	TCA Ser -30	AAG Lys	GAT Asp	CTC Leu	CCT Pro	CAC His -25	TGG Trp	AAC Asn	AAG Lys	CTT Leu	AAA Lys -20	GCA Ala	GAT Asp	GAG Glu	295
AAG Lys	TAC Tyr -15	TTC Phe	ATC Ile	TCT Ser	CAC His	ATC Ile -10	TTA Leu	GCC Ala	TTT Phe	TTT Phe	GCA Ala -5	GCC Ala	AGT Ser	GAT Asp	GGA Gly	343
ATT Ile I	GTA Val	AAT Asn	GAA Glu	AAT Asn 5	TTG Leu	GTG Val	GAG Glu	CGC Arg	TTT Phe 10	AGT Ser	CAG Gln	GAG Glu	GTG Val	CAG Gln 15	GTT Val	391
CCA Pro	GAG Glu	GCT Ala	CGC Arg 20	TGT Cys	TTC Phe	TAT Tyr	GGC Gly	TTT Phe 25	CAA Gln	ATT Ile	CTC Leu	ATC Ile	GAG Glu 30	AAT Asn	GTT Val	439
CAC His	TCA Ser	GAG Glu 35	ATG Met	TAC Tyr	AGT Ser	TTG Leu	CTG Leu 40	ATA Ile	GAC Asp	ACT Thr	TAC Tyr	ATC Ile 45	AGA Arg			481

# (2) INFORMATION FOR SEQ ID NO: 126:

- (1) SEQUENCE CHARACTERISTICS:
  - (A) LENGTH: 197 base pairs
  - (B) TYPE: NUCLEIC ACID
  - (C) STRANDEDNESS: DOUBLE
  - (D) TOPOLOGY: LINEAR
- (ii) MOLECULE TYPE: CDNA
- (vi) ORIGINAL SOURCE:
  - (A) ORGANISM: Homo Sapiens
  - (F) TISSUE TYPE: Brain
- (ix) FEATURE:
  - (A) NAME/KEY: sig\_peptide (B) LOCATION: 3..50

  - (C) IDENTIFICATION METHOD: Von Heijne matrix
  - (D) OTHER INFORMATION: score 4.4

seq GLFSLLPHPPCVG/RV

(mi) SEQUENCE DESCRIPTION: SEQ ID NO: 126:

AG ATG GAT GCA GGC TTA TIT TOT CTG CTT CCC CAT CCT CCA TGT GTT Met Asp Ala Gly Leu Ing Ser Leu Leu Pro His Pro Pro Cys Val 47 -10 **~** 5

GGC ACC GTG CCA CAC TOT AGG TAT CAT CTG CAT CCA AGA TOA CCT

									9	5			·			
Gly	Arg 1	Val	Leu	Pro	G1n 5	Ser	Arg	Tyr	His	Leu 10	His	Pro	Arg	Ser	Pro 15	
					TGT Cys											143
AAA Lys	ATA Ile	GGA Gly	AAC Asn 35	CTT Leu	TTC Phe	CAT His	TCA Ser	ACA Thr 40	AAG Lys	TCC Ser	CTT Leu	TGT Cys	GTC Val 45	TCA Ser	CTT Leu	191
	CCG Pro															197
(2)	(; (,	i) SI ii)   vi) (	EQUEI (A) (B) (C) (D) MOLE (A) (F) FEAT (A) (B) (C) (D)	NCE ( LENG TYPE STRI TOPE CULE INAL ORG. TIS. URE: NAM LOC IDE OTH	SEQ CHARA GTH: E: NU ANDEL DLOG' TYPI SOUI ANISI SUE ' E/KE ATIO NTIF ER I	ACTEI 121 ICLEI DNESS Y: LI E: CI RCE: H: HG IYPE Y: S. N: GI ICAT NFOR	DNA  ig_p  ig_p  indicate  MATI	ICS: e pai CID DUBLE R Sapi ain epti 06 METH	ens de OD: sco seq	re 4 LIT	.4 LTYL	IQGE				
ATT	TAAT	AAC	TTAA	AAAT	TG G	CCAA	тттт	'А ТТ	TTTA	.GAAA	AGC	тстс	CAT	CATO	CTGTG	T 60
TTA						u Th				e Gl					CA CGA La Arg	ī
		TTC Phe		ı												121
(2)	<b>{</b>		SEQUE (A) (B) (C) (D)	ENCE LEN TYPE STE TO	CHAR GTH: PE: 1 RANDE	RACTE 238 UCLE DNES	ERIST B bas EIC A ES: E	rics: se pa ACID	irs							

WO 99/06552 99 PCT/IB98/01236

<ul><li>(vi) ORIGINAL SOURCE:</li><li>(A) ORGANISM: Homo Sapiens</li><li>(F) TISSUE TYPE: Brain</li></ul>	
<pre>(ix) FEATURE:     (A) NAME/KEY: sig_peptide     (B) LOCATION: 146223     (C) IDENTIFICATION METHOD: Von Heijne matrix     (D) OTHER INFORMATION: score 4.4     seq RVQCLCAIPFAFS/LT</pre>	
(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 128:	
AAAATATGTC TTCAGCTCTA ATCCATTATC ACTCAGATCA TTCTAACCTT TTCCCCTTGC	60
TTATCTATAA CTTTCCACTT CAACAGTGAG AAACCTGGCT TCCATATCTG TCATCCATAA	120
ATGTACGTAT TTAATTCCAG TACAC ATG TAT ACT GGT TTC AGA ATA GAA GCA  Met Tyr Thr Gly Phe Arg Ile Glu Ala  -25  -20	172
ACT TTA TTA ACT AGA GTG CAG TGC TTA TGT GCA ATT CCT TTT GCC TTT Thr Leu Leu Thr Arg Val Gln Cys Leu Cys Ala Ile Pro Phe Ala Phe -15 -5	220
AGT CTT ACA GGC ATC CGG Ser Leu Thr Gly Ile Arg 1 5	238
(2) INFORMATION FOR SEQ ID NO: 129:  (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 419 base pairs (B) TYPE: NUCLEIC ACID (C) STRANDEDNESS: DOUBLE (D) TOPOLOGY: LINEAR  (ii) MOLECULE TYPE: CDNA  (vi) ORIGINAL SOURCE: (A) ORGANISM: Homo Sapiens (F) TISSUE TYPE: Brain  (ix) FEATURE: (A) NAME/KEY: sig_peptide (B) LOCATION: 252392 (C) IDENTIFICATION METHOD: Von Heijne matrix (D) OTHER INFORMATION: score 4.4 seq ISHILAFFAASDG/IV	
(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 129:	
AAGUSSACCA CCTGGGTGCT GTCGTAGTTG GAGGTGGCCT GAGGAGCTCA GTTCCCTCAG	60
USSNOSTAGT TTCGGCGGAG TCTGCGCGAT GGGCGACCCG GAAAGGCCGG CAAGGCCAA	60 20

	100
GGCTGGATCA GGATGAGAGA TCATCTTCAG AC	ACCAACGA AAGTGAAATA AAGTCAAATG 180
AAGAGCCRST CCTAAGAAAG AGTTCTCGCC GC	STTTGTCAT CTTTCCAATC CAGTACCCTG 240
ATATTTGGAA A ATG TAT AAA CAG GCA CA Met Tyr Lys Gln Ala Gl -45	AG GCT TCC TTC TGG ACA GCA GAA 290 In Ala Ser Phe Trp Thr Ala Glu -40 -35
GAG GTC GAC TTA TCA AAG GAT CTC CCT Glu Val Asp Leu Ser Lys Asp Leu Pro -30	CAC TGG AAC AAG CTT AAA GCA 338 His Trp Asn Lys Leu Lys Ala -25 -20
GAT GAG AAG TAC TTC ATC TCT CAC ATC ASp Glu Lys Tyr Phe Ile Ser His Ile -15	Leu Ala Phe Phe Ala Ala Ser .
GAT GGA ATT GTA AAT GAA AAT TTG GTG Asp Gly Ile Val Asn Glu Asn Leu Val	
(2) INFORMATION FOR SEQ ID NO: 130	
(i) SEQUENCE CHARACTERISTICS:  (A) LENGTH: 255 base pa  (B) TYPE: NUCLEIC ACID  (C) STRANDEDNESS: DOUBI  (D) TOPOLOGY: LINEAR	nirs
(ii) MOLECULE TYPE: CDNA	
<pre>(vi) ORIGINAL SOURCE:     (A) ORGANISM: Homo Sapi     (F) TISSUE TYPE: Brain</pre>	lens
<pre>(ix) FEATURE:     (A) NAME/KEY: sig_pept:     (B) LOCATION: 112195     (C) IDENTIFICATION MET!     (D) OTHER INFORMATION:</pre>	HOD: Von Heijne matrix
(xi) SEQUENCE DESCRIPTION: S	EQ ID NO: 130:
AATTACGATG TKKTGTGTGC TTGTGCAAAT A	CAGGACGGT TCCTGAAATG TGTCTCTGAG 60
CGTTCTTAAC TGTGTGTRAG GAATTSMTGC G	CGTACACGT GGTGGGTCAT T ATG CTG 117 Met Leu
CTG CAC CTG TGT AGT GTG AAG AAT CT Leu His Leu Cys Ser Val Lys Asn Le -25 -20	G TAC CAG AAC AGG TTT TTA GGC 169 u Tyr Gln Asn Arg Phe Leu Gly -15
CTG GCC GCC ATG GCG TCT CCT TCT AG Leu Ala Ala Met Ala Ser Pro Ser Ar -10	
TGC AAG GAG CCG CTC CGA TAC AGC TAC	

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10	15	20	

(2) INFORMATION FOR SEQ ID NO: 131:	
(i) SEQUENCE CHARACTERISTICS:  (A) LENGTH: 287 base pairs  (B) TYPE: NUCLEIC ACID  (C) STRANDEDNESS: DOUBLE  (D) TOPOLOGY: LINEAR	
(ii) MOLECULE TYPE: CDNA	
<pre>(vi) ORIGINAL SOURCE:     (A) ORGANISM: Homo Sapiens     (F) TISSUE TYPE: Brain</pre>	٠
<pre>(ix) FEATURE:     (A) NAME/KEY: sig_peptide     (B) LOCATION: 123176     (C) IDENTIFICATION METHOD: Von Heijne matrix     (D) OTHER INFORMATION: score 4.3</pre>	
(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 131:	
AAGAGCATCC TGCGCCCCGG CGCGGGGCCC TGCGGTAGCC TCAGGCCCCT CCCCTGGACC	60
CGCCGCAGAG CCAGTGCAGA ATACAGAAAC TGCAGCCATG ACCACGCACG TCACCCTGGA	120
AG ATG CCC TGT CCA ACG TGG ACC TGC TTG AAG AGC TTC CCC TCC CCG	
Met Pro Cys Pro Thr Trp Thr Cys Leu Lys Ser Phe Pro Ser Pro  -15 -10 -5	167
ACC AGC AGC CAT GCA TCG AGC CTC CAC CTT CCT CCA TCA TGT ACC AGG Thr Ser Ser His Ala Ser Ser Leu His Leu Pro Pro Ser Cys Thr Arg 1 5 10	215
CTA ACT TTG ACA CAA ACT TTG AGG ACA GGA ATG CAT TTG TCA CGG GCA Leu Thr Leu Thr Gln Thr Leu Arg Thr Gly Met His Leu Ser Arg Ala 15 20 25	263
TTG CAA GGT ACA TTG ACC AGG CAG Leu Gln Gly Thr Leu Thr Arg Gln 30 35	287
(2) INFORMATION FOR SEQ ID NO: 132:	
(i) SEQUENCE CHARACTERISTICS:  (A) LENGTH: 224 base pairs  (B) TYPE: NUCLEIC ACID  (C) STRANDEDNESS: DOUBLE  (D) TOPOLOGY: LINEAR	

(ii) MOLECULE TYPE: CDNA
(vi) OBIGINAL SOURCE:

(A)	ORGANIS	SM: Ho	omo	Sapiens
(F)	TISSUE	TYPE:	: Bı	rain

#### (ix) FEATURE:

- (A) NAME/KEY: sig\_peptide
- (B) LOCATION: 6..104
- (C) IDENTIFICATION METHOD: Von Heijne matrix

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(D) OTHER INFORMATION: score 4.3

seq LLGWGLNLTLGQG/AP

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 132:

AAAGG ATG GAG GAT CTC TTT AGC CCC TCA ATT AWG CCG CCG GCG CCC AAC Met Glu Asp Leu Phe Ser Pro Ser Ile Xaa Pro Pro Ala Pro Asn -30-25

ATT TCC GTG CCC ATC TTG CTG GGC TGG GGT CTC AAC CTG ACC TTG GGG 98 Ile Ser Val Pro Ile Leu Leu Gly Trp Gly Leu Asn Leu Thr Leu Gly -15 -10

CAA GGA GCC CCT GCC TCT GGG CCG CCC AGC CGC CGC GTC CGC CTG GTG 146 Gln Gly Ala Pro Ala Ser Gly Pro Pro Ser Arg Arg Val Arg Leu Val

TTC CTG GGG GTC ATC CTG GTG GTG GCG GTG GCA KGC AAC ACC ACA GTG Phe Leu Gly Val Ile Leu Val Val Ala Val Ala Xaa Asn Thr Thr Val 15 .20 25

CTG TGC CGC CTG TGC GGC GGC GGC CCG 224 Leu Cys Arg Leu Cys Gly Gly Gly Pro

#### (2) INFORMATION FOR SEQ ID NO: 133:

- (i) SEQUENCE CHARACTERISTICS:
  - (A) LENGTH: 347 base pairs
  - (B) TYPE: NUCLEIC ACID
  - (C) STRANDEDNESS: DOUBLE
  - (D) TOPOLOGY: LINEAR
- (ii) MOLECULE TYPE: CDNA
- (vi) ORIGINAL SOURCE:
  - (A) ORGANISM: Homo Sapiens
  - (F) TISSUE TYPE: Brain
- (ix) FEATURE:
  - (A) NAME/KEY: sig\_peptide
  - (B) LOCATION: 183..338
  - (C) IDENTIFICATION METHOD: Von Heijne matrix
  - (D) OTHER INFORMATION: score 4.1

seq VMLETCGLLVSLG/HP

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 133:

WO 99/06552 103	PC1/1B/G/O
AGAACTGTGC TGGGAAGGAT GGTAGGGGGA CTGGGGGCTCA CCTCCGCACC GT	TGTAGGAC 120
CCGGGGTAGG GTTTTGAGCC CGTGGGAGCK GCCCCACGCG GCCTCSTCCT GCC	CAACGGTC 180
GG ATG GCG GAG ACG AAG GAC GCA GCG CAG ATG TTG GTG ACC TTG Met Ala Glu Thr Lys Asp Ala Ala Gln Met Leu Val Thr Phe	
GAT GTG GCT GTG ACC TTT ACC CGG GAG GAG TGG AGA CAG CTG GA Asp Val Ala Val Thr Phe Thr Arg Glu Glu Trp Arg Gln Leu As -35 -30 -25	
GCC CAG AGG ACC CTG TAC CGA GAG GTG ATG CTG GAG ACC TGT GG Ala Gln Arg Thr Leu Tyr Arg Glu Val Met Leu Glu Thr Cys G. -20 -15 -10	
CTG GTT TCA CTA GGG CAT CCT CGG Leu Val Ser Leu Gly His Pro Arg -5	347
(2) INFORMATION FOR SEQ ID NO: 134:	
(i) SEQUENCE CHARACTERISTICS:  (A) LENGTH: 432 base pairs  (B) TYPE: NUCLEIC ACID  (C) STRANDEDNESS: DOUBLE  (D) TOPOLOGY: LINEAR	
(ii) MOLECULE TYPE: CDNA	
<pre>(vi) ORIGINAL SOURCE:     (A) ORGANISM: Homo Sapiens     (F) TISSUE TYPE: Brain</pre>	
<pre>(ix) FEATURE:     (A) NAME/KEY: sig_peptide     (B) LOCATION: 298336     (C) IDENTIFICATION METHOD: Von Heijne matrix     (D) OTHER INFORMATION: score 4.1</pre>	
(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 134:	
AATTGARRIG TITGATAACT GICACTITAG GGITTCAACC AAAACCTIGA CI	TTATCATC 60
FIGTTATACA TTTTTCAAAA TGAGGTTAGA GATCAGGGGA ATGAATAGGA GA	AGAAGTACA 120
TATTTCAGTT CACTGGGCAT AGGTGAATAG AGGAAGGAGA AAATGAACAT AC	CCCAATCCA 180
CAGAGAAATG GCTCACAGAG CCCAGTGACT ATGCTGAGAC GCTATTAATT CA	AAGAAAGTT 240
TTAGTATTIG ATTITICARA TGACATTATI GTTTAGGACT TTTATTTTCC CT	TTACAG 297
ATG TTG ATC TO TOT CAG AAT ATT GCC CAA CTG GAG GUC CAG C Met Leu Ile Loo Ser Gin Asn Ile Ala Gln Leu Glu Ala Gln V -10 -5 1	

AAG GTT ACA FI GAA AAG ATT TOA GCT ATT AAT CAA CTG GAG GAA AAT 393

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Lys	Val 5	Thr	Lys	Glu	Lys	Ile 10	Ser	Ala	Ile	Asn	Gln 15	Leu	Glu	Glu .	Asn	
											TCA Ser					432
(2)	INFO	RMAT	ION	FOR	SEQ	ID N	0: 1	35:								
	(i	) SE	(A) (B) (C)	LENG TYPE STRA	HARA TH: : NU NDED LOGY	380 CLEI NESS	base C AC : DO	pai ID UBLE								
	(i	i) M	OLEC	ULE	TYPE	: CD	NA									
	( v	i) O	(A)	ORGA	SOUR NISM UE T	: Но			ns							
	(i	ж) F	(B) (C)	NAME LOCA IDEN	KEY TION TIFI R IN	: 90 CATI	15 ON M	2 IETHO	D: V	e 4.	leijn 1 \HSWT					
	( x	i) S	EQUE	ENCE	DESC	RIPT	'ION:	SEC	) ID	NO:	135:					
AATI	CACT	TC P	ACCT(	GGAGI	rt g <i>i</i>	AGCC#	\AGA1	r TCT	CTT	TACT	CCA	<b>A</b> GCC	CAG C	CACTO	CTTCT	60
GAG	ACAG	GA (	PHTT	GATT!	rg ga	ATGG?	ACGG				GGG Gly					113
Gly	Leu	Trp	Ala	His	Ser	Trp	Thr	Cys	Ser	Cys	TCA Ser	Ala	Ala	Xaa		161
											TTT Phe 15					209
											ACA Thr					257
		•			Leu					Leu	GAG Glu					305
				Asp					Thr		TAT Tyr			Asn		353

380

ATT TCA GAA TGT ACG TTT TCC TTT TTT Ile Ser Glu Cys Thr Phe Ser Phe Phe

WO 99/06552		PCT/IB98/01236
11 0 7 7 00 3 3 2	105	

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(2) INFORMATION FOR SEQ ID NO: 136:	
(i) SO, WENCE CHARACTERISTICS:  (A) LENGTH: 212 base pairs  (B) TYPE: NUCLEIC ACID  (C) STRANDEDNESS: DOUBLE  (D) TOPOLOGY: LINEAR	
(ii) MOLECULE TYPE: CDNA	
<ul><li>(vi) ORIGINAL SOURCE:</li><li>(A) ORGANISM: Homo Sapiens</li><li>(F) TISSUE TYPE: Brain</li></ul>	
<pre>(ix) FEATURE:     (A) NAME/KEY: sig_peptide     (B) LOCATION: 953     (C) IDENTIFICATION METHOD: Von Heijne matrix     (D) OTHER INFORMATION: score 4.1     seq APLELSCWGGGWG/LP</pre>	
(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 136:	
AGCGCAAG ATG GCG GCC CCC TTG GAA CTC AGT TGC TGG GGA GGC GGC TGG  Met Ala Ala Pro Leu Glu Leu Ser Cys Trp Gly Gly Trp  -15 -10 -5	50
GGA CTC CCA TOG GTT CAC AGO GAG TCC CTG GTG GTG ATG GCT TAT GCC Gly Leu Pro Ser Val His Ser Glu Ser Leu Val Val Met Ala Tyr Ala 1 5 10	98
AAA TTT TCT GGT GCA CCC TTG AAA GTC AAT GTG ATA GAT AAC ACC TGG Lys Phe Ser Gly Ala Pro Leu Lys Val Asn Val Ile Asp Asn Thr Trp 20 25 30	146
AGA GGT TCR AGA GGC GAT GTA CCA ATT TTG ACA ACT GAA GAC GAC ATG Arg Gly Ser Arg Gly Asp Val Pro Ile Leu Thr Thr Glu Asp Asp Met 35 40 45	194
GTT TCT CAG CCA GCA AGG Val Ser Gin Pro Ala Arg 50	212
(2) INFORMATION FOR SEQ ID NO: 137:	
(i) SETTENCE CHARACTERISTICS:  (ii) LENGTH: 432 base pairs  (iii) TYPE: NUCLEIC ACID  (i) STRANDEDNESS: DOUBLE  (ii) TOPOLOGY: LINEAR	

- (ii) NoveCule Type: CDNA
- (vi FIBINAL SOURCE:

(A) ORGANISM: Homo Sapiens (F) TISSUE TYPE: Brain

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- 1	1 Y	1 -	 - "	* 1	H H	•
٠,		, .	 7 7	v	***	•

(A) NAME/KEY: sig\_peptide

- (B) LOCATION: 226..285
- (C) IDENTIFICATION METHOD: Von Heijne matrix

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(D) OTHER INFORMATION: score 4.1

seq LGFLNCYIAVARS/GG

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 137:

AAGGGAMNSA CCCAGGCTGC GGGACSGGTG CAGGCTGCGG CGCTGACGGC CTCTGCTCCT 60 TCCGCGGGTT TCCGACTCCC TGCCCTAGAT TTTCTGCTTA GCGACTTGGG GTCCCCTCTC 120 GTTTGCTTCT GGTAGGAGTC GCAATCCCAK BAGCAATAGC CCAGAAGAGG ACACGGTTCC CGTACCGAAG GTTCAGTACC AGCAGCCCGA CCATCACGCG GCGGG ATG TCT GDR GTT Met Ser Xaa Val -20 GGC ATT GAC CTC GGC TTT CTC AAC TGC TAC ATT GCT GTC GCG AGA AGT 285 Gly Ile Asp Leu Gly Phe Leu Asn Cys Tyr Ile Ala Val Ala Arg Ser -15 GGC GGC ATC GAG ACC ATC GCC AAT GAG TAC AGC GAC AGG TGT ACC CCG 333 Gly Gly Ile Glu Thr Ile Ala Asn Glu Tyr Ser Asp Arg Cys Thr Pro 10 GCC TGT ATA TCA TTG GGA TCA AGA ACT CGA GCC ATT GGA AAT GCA GCA Ala Cys Ile Ser Leu Gly Ser Arg Thr Arg Ala Ile Gly Asn Ala Ala 20 30 AAG AGC CAG ATA GTC ACG AAC GTA AGA AAT ACA ATT CAT GGC TTC AAA 429 Lys Ser Gln Ile Val Thr Asn Val Arg Asn Thr Ile His Gly Phe Lys 35 AAG 432 Lys

## (2) INFORMATION FOR SEQ ID NO: 138:

- (i) SEQUENCE CHARACTERISTICS:
  - (A) LENGTH: 229 base pairs
  - (3) TYPE: NUCLEIC ACID
  - (C) STRANDEDNESS: DOUBLE
  - (D) TOPOLOGY: LINEAR
- (ii) MOLECULE TYPE: CDNA
- (vi) (RIGINAL SOURCE:
  - (A) ORGANISM: Homo Sapiens
  - (F) TISSUE TYPE: Brain
- (ix) FEATURE:
  - (A) NAME/KEY: sig\_peptide
  - (B) LOCATION: 101..157

(C) IDENTIFICATION METHOD: Von Heijne matrix (D) OTHER INFORMATION: score 4.1 seq FVVFSTMFTASSP/GE	
(x1) SEQUENCE DESCRIPTION: SEQ ID NO: 138:	
AGATGAATAT TIGATACCCA CAGTAGAACT TCTTTMMGAA CTTCTTTCAC AATWGGAGTT	60
AATCTTCTAA AGCCCCGCCA CTGCTTCATC AACTAAGTTT ATG GAA TAT TCT AAA Met Glu Tyr Ser Lys -15	115
TMM TTT GTT GTC TTT TCA ACA ATG TTC ACA GCA TCT TCA CCA GGA GAA Xaa Phe Val Val Phe Ser Thr Met Phe Thr Ala Ser Ser Pro Gly Glu -10 -5 1	163
GAC TTT CCC CCC TTC TTT TCA CAG ATG TNS AGA TTG TCA AGA AAC TAC Asp Phe Pro Pro Phe Phe Ser Gln Met Xaa Arg Leu Ser Arg Asn Tyr 5 10 15	211
TTT CCT TGC CCA CCR WGG Phe Pro Cys Pro Pro Xaa 20	229
(2) INFORMATION FOR SEQ ID NO: 139:  (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 328 base pairs (B) TYPE: NUCLEIC ACID (C) STRANDEDNESS: DOUBLE (D) TOPOLOGY: LINEAR  (i1) MOLECULE TYPE: CDNA  (vi) ORIGINAL SOURCE: (A) ORGANISM: Homo Sapiens (F) TISSUE TYPE: Brain  (ix) FEATURE: (A) NAME/KEY: sig_peptide (B) LOCATION: 113232 (C) IDENTIFICATION METHOD: Von Heijne matrix (D) OTHER INFORMATION: score 4.1 seq_LPERLPWASTATA/RC	
AACACCCAGO CCCTGATGCA GCAGCAGGCG GCCCTGGTAG CGGCTCACAG TGCCTACCTC	60
AGCCCCATRU CCACCATGCC TGCCGTGCAG ATGCAGCACA TGGCTGCCAT CA ATG CCA Met Pro -40	118
ATG GCC TCD TCG CCA CCC CCA TCA CCC CAT CCT CAG GAA CCA GCA CCC Met Ala Jer Ser Pro Pro Pro Ser Pro His Pro Gln Glu Pro Ala Pro -35 -25	166

WO 99/06552 PCT/IB98/01236

WO 99/00332		10	8		2,120,000
CTC CTG CCA TCG Leu Leu Pro Ser -20	Leu Pro Arg 1				214
GCG TCA ACG GCT Ala Ser Thr Ala -5					262
CNC CTG ATG CTC Xaa Leu Met Leu					310
GCC CCG CGG CCC Ala Pro Arg Pro 30	Pro Gly				328
(2) INFORMATION FOR SEQ ID NO: 140:  (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 217 base pairs (B) TYPE: NUCLEIC ACID (C) STRANDEDNESS: DOUBLE (D) TOPOLOGY: LINEAR  (ii) MOLECULE TYPE: CDNA  (vi) ORIGINAL SOURCE: (A) ORGANISM: Homo Sapiens (F) TISSUE TYPE: Brain  (ix) FEATURE: (A) NAME/KEY: sig_peptide (B) LOCATION: 53166 (C) IDENTIFICATION METHOD: Von Heijne matrix (D) OTHER INFORMATION: score 4 seq WALGLKFLSSSSQ/NF  (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 140:					
AACAGGAGAC TTGG	GAAGGA CCAATO	GGTAA TTTAAG	TGGC TCTTAAA	AAG TC ATG CA Met Gl	
CAT GTW WCT GGA					106

CAT GTW WCT GGA CAC GWW CCT GAT CCT ATT GCG ATA ATG TAT GTG TGC
His Val Xaa Gly His Xaa Pro Asp Pro Ile Ala Ile Met Tyr Val Cys
-35

CCT CCC TGT GGG CAC ACC ACC TGG GCA TTA GGA CTG AAA TTC CTG AGT
Pro Pro Cys Gly His Thr Thr Trp Ala Leu Gly Leu Lys Phe Leu Ser
-20

TCT TCC TCT CAA AAT TTC TGT GCA CCA GTA TTA TTC CTC ATT TTA CAT
Ser Ser Wer Gln Asn Phe Cys Ala Pro Val Leu Phe Leu Ile Leu His
1

ACA GGA GGC CAA CGG
Thr Gly Gly Gln Arg
15

	10)	
(2)	INFORMATION FOR SEQ ID NO: 141:	
	<ul> <li>(i) SEQUENCE CHARACTERISTICS:</li> <li>(A) LENGTH: 202 base pairs</li> <li>(B) TYPE: NUCLEIC ACID</li> <li>(C) STRANDEDNESS: DOUBLE</li> <li>(D) TOPOLOGY: LINEAR</li> </ul>	
	(ii) MOLECULE TYPE: CDNA	
	<ul><li>(vi) ORIGINAL SOURCE:</li><li>(A) ORGANISM: Homo Sapiens</li><li>(F) TISSUE TYPE: Brain</li></ul>	
	(ix) FEATURE: (A) NAME/KEY: sig peptide	

(B) LOCATION: 44..133

(C) IDENTIFICATION METHOD: Von Heijne matrix

(D) OTHER INFORMATION: score 4 seq AGFLKCLLLSSLQ/SY

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 141:

ATA	ATAG	TGT	TATT	TCAG	TG C	ATGA	TTTT	T GC	CTTT	GAGA	GAC	ATG Met	Gly	TGG Trp	GAA Glu	55
	-25			-		-20	1110	тър	мта	AGG Arg	Ser -15	His	Ala	Gly	Phe	103
-10					-5	- • •	001	Leu	GIN	TCC Ser l	Tyr	Lys	Glu	Ala 5	Ala	151
GTT Val	ATC Ile	TTC Phe	CCT Pro 10	CTT Leu	ACT Thr	GAT Asp	TTG Leu	CTC Leu 15	AAA Lys	CTG Leu	AAA Lys	GAT Asp	TAT Tyr 20	GGT Gly	GAA Glu	199
TGG Trp																202

# (2) INFORMATION FOR SEQ ID NO: 142:

- (i) SEQUENCE CHARACTERISTICS:
  - (A) LENGTH: 361 base pairs
  - (3) TYPE: NUCLEIC ACID
  - (C) STRANDEDNESS: DOUBLE
  - (0) TOPOLOGY: LINEAR
- (11) MOLECULE TYPE: CDNA
- TVI) ORIGINAL SOURCE:
  - (A) ORGANISM: Homo Sapiens
    (F) TISSUE TYPE: Brain

<pre>(ix) FEATURE:     (A) NAME/KEY: sig_peptide     (B) LOCATION: 248355     (C) IDENTIFICATION METHOD: Von Heijne matrix     (D) OTHER INFORMATION: score 4</pre>	
(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 142:	
AAGTTGGGAG AGGAGCTGCT GGTTGAAGTG AAGGTGAGGA GCTCAGTGCT TCTTTCACTG	60
CCCTATCTGC TGGGCTTTAC GCCCCTGAGG GGCTGACTGT AAAAAACTCT AAGCTGATCC	120
AGCCCCCAAA ATTCACCTTT GGTGAGCTGG AAAGTCCATC TATTTGGGAC GCGAATCATG	180
TCAGTGCGAC AACGCAAAAG GGTTGAAAGC CTTCTACGAT GCAATAAAAT ACGGGCCTAA	240
CCACTTG ATG GTG TTT GGA GGC GTC TGT CCA TCC GTC ACA TCC ATT  Met Val Phe Gly Gly Val Cys Pro Ser Val Thr Ser Ile Ile  -35 -30 -25	289
GCA GAG TCC CTC CAA GGC TGG AAT CTG GTG CAG CTT TCT TTT GCT GCA Ala Glu Ser Leu Gln Gly Trp Asn Leu Val Gln Leu Ser Phe Ala Ala -20 -15 -10	337
ACC ACG CCT GTT CTA GCC GAT AAG Thr Thr Pro Val Leu Ala Asp Lys -5 1	361
(2) INFORMATION FOR SEQ ID NO: 143:  (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 216 base pairs (B) TYPE: NUCLEIC ACID (C) STRANDEDNESS: DOUBLE (D) TOPOLOGY: LINEAR  (ii) MOLECULE TYPE: CDNA  (vi) ORIGINAL SOURCE: (A) ORGANISM: Homo Sapiens (F) TISSUE TYPE: Brain  (ix) FEATURE: (A) NAME/KEY: sig_peptide (B) LOCATION: 145192 (C) IDENTIFICATION METHOD: Von Heijne matrix (D) OTHER INFORMATION: score 4 seq ITWSLLFLYQCSL/HF  (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 143:	
ACACATTACC TCTTTCATT TTAGACAGGT TAATTAGTGT GTATTTCCAT AGTTGTCTTT	60
TACCTCAAGA AATAATCATT TCTTTAGGTA ATTATTTTAA TGGCTTGCCA TTTTGTATGA	120

TTGTTGTTGC AAACATTTCT ATTT ATG CAT TTT ATA ACA TGG AGC TTA CTA 171

Met His Phe Ile Thr Trp Ser Leu Leu -15 -10

TTT TTA TAC CAG TGC TCG CTT CAT TTT ATC ATT ATC AAG GCC GGG Phe Leu Tyr Gln Cys Ser Leu His Phe Ile Ile Lys Ala Gly 216 1

- (2) INFORMATION FOR SEQ ID NO: 144:
  - (i) SEQUENCE CHARACTERISTICS:
    - (A) LENGTH: 378 base pairs
    - (B) TYPE: NUCLEIC ACID
    - (C) STRANDEDNESS: DOUBLE
    - (D) TOPOLOGY: LINEAR
  - (ii) MOLECULE TYPE: CDNA
  - (vi) ORIGINAL SOURCE:
    - (A) ORGANISM: Homo Sapiens
    - (F) TISSUE TYPE: Brain
  - (ix) FEATURE:
    - (A) NAME/KEY: sig\_peptide
    - (B) LOCATION: 256..363
    - (C) IDENTIFICATION METHOD: Von Heijne matrix
    - (D) OTHER INFORMATION: score 3.9 seq CWPSVASPSSSWS/SP
  - (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 144:

AAASTGGCCA GCGGACCATC TCTCGTGCCC TCGCTCTCTG CGCTCCGGGG CAGCTGAGCC 60

CCGGCCACCC GCTCTCCAAG ATGAAGAAGC TCCAGGGAGC TCACCTCCGC AAGCCTGTCA 120

CCCCAGACCT GCTGATGACC CCCAGTGACC AGGGCGATGT CGACCTGGAT GTGGACTTTG

CTGCACACCG GGGGAACTGG ACAGGCAAGC TGGACTTCCT GCTGTCCTGC ATTGGCTACT

GTGTAGGCCT GGGGA ATG TCT GGC GCT TCC CCT ATC GAG CGT ACA CCA ATG Met Ser Gly Ala Ser Pro Ile Glu Arg Thr Pro Met 291 -30

GAG GAG GCG CCT TCC TCG TGC CCT ACT TCC TCA TGC TGG CCA TCT GTG Glu Glu Ala Pro Ser Ser Cys Pro Thr Ser Ser Cys Trp Pro Ser Val 339 -15

GOA TOO CCC TCT TCT TCC TGG AGC TCT CCC TGG GCC AGT Ara Ser Pro Ser Ser Ser Trp Ser Ser Pro Trp Ala Ser 378 1

- (2) IMFORMATION FOR SEQ ID NO: 145:
  - (i) SEQUENCE CHARACTERISTICS:
    - (A) LENGTH: 321 base pairs
    - (B) TYPE: NUCLEIC ACID
    - (C) STRANDEDNESS: DOUBLE

(D)	TOPO	LOGY:	LINEAR
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- (ii) MOLECULE TYPE: CDNA
- (vi) ORIGINAL SOURCE:
  - (A) ORGANISM: Homo Sapiens
  - (F) TISSUE TYPE: Brain
- (ix) FEATURE:
  - (A) NAME/KEY: sig\_peptide
  - (B) LOCATION: 172..282
  - (C) IDENTIFICATION METHOD: Von Heijne matrix
  - (D) OTHER INFORMATION: score 3.9

seq PGPSLRLFSGSQA/SV

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 145:

AAGGGTCTCC ATGACAACCG GCCTGGCCGG CTAGCAGTGC TCTGCTCACT TGGCTGCGAG 60

GAGCGCCACG AAAGGTCAGA GGAAGGAGCT GTGGGAAGCT CGCAGCAGGT ATCGGAGCTT 120

AAGCCAGTGG ATTTGGGGGC CCTGGGCTCC CTAGCCGGCT GCGGTGTGAG A ATG GAG 177 Met Glu

TGG GCA GGA AAG CAG CGG GAC TTT CAG GTA AGG GCA GCT CCG GGC TGG 225 Trp Ala Gly Lys Gln Arg Asp Phe Gln Val Arg Ala Ala Pro Gly Trp -35 -30 -25

GAT CAT TTG GCC TCC TTT CCT GGC CCT TCT CTC CGG CTG TTT TCT GGG 273 Asp His Leu Ala Ser Phe Pro Gly Pro Ser Leu Arg Leu Phe Ser Gly -15 -10

AGT CAG GCG AGT GTC TGT AGT CTC TGC TCG GGG TTT GGG GCT CAG GAA 321 Ser Gln Ala Ser Val Cys Ser Leu Cys Ser Gly Phe Gly Ala Gln Glu

# (2) INFORMATION FOR SEQ ID NO: 146:

- (i) SEQUENCE CHARACTERISTICS:
  - (A) LENGTH: 278 base pairs
  - (B) TYPE: NUCLEIC ACID
  - (C) STRANDEDNESS: DOUBLE
  - (D) TOPOLOGY: LINEAR
- (ii) MOLECULE TYPE: CDNA
- (vi) ORIGINAL SOURCE:
  - (A) ORGANISM: Homo Sapiens
  - (F) TISSUE TYPE: Brain
- (ix) FEATURE:
  - (A) NAME/KEY: sig\_peptide
  - (B) LOCATION: 78..257
  - (C) IDENTIFICATION METHOD: Von Heijne matrix
  - (D) OTHER INFORMATION: score 3.9

seq AKVVSLSLQTSSA/HH

(Mi) SEQUENCE DESCRIPTION: SEQ ID NO: 146:

Par Pachon	
AAGAACACAA AAAGCTACAG AAGGTCCAGG CTACTGAAAA GCATCAAGAC CAAGCTGTTG	60
TAAGTCAAAC TGCTTTT ATG ATT GCA TTC TTT GAT GAA GAC AAT CCC AGA  Met Ile Ala Phe Phe Asp Glu Asp Asn Pro Arg  -60  -55 -50	110
AAA AGA AGG TCG TAT TCT TTT ACT CAA AGT GCG GGA ATC TTG TGT CAG Lys Arg Arg Ser Tyr Ser Phe Thr Gln Ser Ala Gly Ile Leu Cys Gln -45 -40 -35	158
GAA ACT ACA TAT TCA ACA CCA CAT ACA AAA CTT GAG AAA GCA AAG TCT Glu Thr Thr Tyr Ser Thr Pro His Thr Lys Leu Glu Lys Ala Lys Ser -30 -25 -20	206
CCA ACA GCA GAT GCC AAA GTG GTT TCT TTG TCT TTA CAG ACT AGC TCT Pro Thr Ala Asp Ala Lys Val Val Ser Leu Ser Leu Gln Thr Ser Ser -15 -5	254
GCG CAT CAC AGA GGG GGG MDT GGT Ala His His Arg Gly Gly Xaa Gly 1 5	278
(2) INFORMATION FOR SEQ ID NO: 147:  (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 349 base pairs (B) TYPE: NUCLEIC ACID (C) STRANDEDNESS: DOUBLE (D) TOPOLOGY: LINEAR  (ii) MOLECULE TYPE: CDNA  (vi) ORIGINAL SOURCE: (A) ORGANISM: Homo Sapiens (F) TISSUE TYPE: Brain  (ix) FEATURE: (A) NAME/KEY: sig_peptide (B) LOCATION: 89232 (C) IDENTIFICATION METHOD: Von Heijne matrix (D) OTHER INFORMATION: score 3.9 seq ALFCTLPCPVERG/QQ  (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 147:	
ARATTITCTT AAATTAGCAG TCTAATGTGT TCTAAAGAGC AGCTCCACTC AGATCTCTTC	<b>6</b> 0
TTAAGGGTTG CATTTCATCA CAGTATAA ATG GGC AAA TCC ATC AYT TCC CTC Met Gly Lys Ser Ile Xaa Ser Leu -45	112
-35 -30 -25	160
TITS IGO TIG CGG GCT CAG AAG CGT CGC ACT GCT TIG TIT IGT ACT	209

WO 99/06552 114 His Leu Cys Leu Arg Ala Gln Lys Arg Arg Thr Ala Leu Phe Cys Thr -20 -15 CTA CCG TGT CCT GTT GAA AGG GGT CAA CAA GTG CCG GGG ANV NNN AHG 256 Leu Pro Cys Pro Val Glu Arg Gly Gln Gln Val Pro Gly Xaa Xaa Xaa -5 1 AGG CTG AGG CTG GCG TCA CCT TCC GTT GCT AAG GTG TTC CAG TGT TTT 304 Arg Leu Arg Leu Ala Ser Pro Ser Val Ala Lys Val Phe Gln Cys Phe 10 15 CTC TCA AAA CTC TGT GTT TGG AAC ATC AAG GAT GGA TTA TCC CGG 349 Leu Ser Lys Leu Cys Val Trp Asn Ile Lys Asp Gly Leu Ser Arg 30 (2) INFORMATION FOR SEQ ID NO: 148: (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 210 base pairs (B) TYPE: NUCLEIC ACID

- (C) STRANDEDNESS: DOUBLE
- (D) TOPOLOGY: LINEAR
- (ii) MOLECULE TYPE: CDNA
- (vi) ORIGINAL SOURCE:
  - (A) ORGANISM: Homo Sapiens
  - (F) TISSUE TYPE: Brain
- (ix) FEATURE:
  - (A) NAME/KEY: sig\_peptide
  - (B) LOCATION: 52..96
  - (C) IDENTIFICATION METHOD: Von Heijne matrix
  - (D) OTHER INFORMATION: score 3.9

seq LHMTLFRVPFTFS/XF

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 148:

ACACAAAGGA AAATGGCAGG GATATGAATT TCTTTCCCAG CTTTTATATA G ATG TGC Met Cys -15	. 57
CTG CAT ATG ACA CTC TTT AGA GTT CCT TTC ACT TTT TCT KTT TTT TGG	105
Leu His Met Thr Leu Phe Arg Val Pro Phe Thr Phe Ser Xaa Phe Trp -10 -5 1	
AAG GGG GCG GGG AGG CAG GAG GAG TGC AGT TTT AAG CCT AGC CTA TAC	153
Lys Gly Ala Gly Arg Gln Glu Glu Cys Ser Phe Lys Pro Ser Leu Tyr 5 10 15	
TAC TAC AAA CTT ATT ATG GTA CTT AAA ATT GCA CTC CTC CTG TCC CCG	201
Tyr Tyr Lys Leu Ile Met Val Leu Lys Ile Ala Leu Leu Leu Ser Pro	
20 25 30 35	
CCC CCC AAG	210
Pro Pro Lys	

(2) INFORMATION FOR SEQ ID NO: 149:	
<ul> <li>(i) SEQUENCE CHARACTERISTICS:</li> <li>(A) LENGTH: 143 base pairs</li> <li>(B) TYPE: NUCLEIC ACID</li> <li>(C) STRANDEDNESS: DOUBLE</li> <li>(D) TOPOLOGY: LINEAR</li> </ul>	
(ii) MOLECULE TYPE: CDNA	
<pre>(vi) ORIGINAL SOURCE:     (A) ORGANISM: Homo Sapiens     (F) TISSUE TYPE: Brain</pre>	
<pre>(ix) FEATURE:     (A) NAME/KEY: sig_peptide     (B) LOCATION: 75116     (C) IDENTIFICATION METHOD: Von Heijne matrix     (D) OTHER INFORMATION: score 3.9</pre>	
(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 149:	
AATACACCTT AAACTTTACT ACTTTTTATA AACGGTAGGA AAGGATATAC TGATGTTGTG	60
GGTATTACAA GGTA ATG CTG AAC ATT CTG AAG ACC TTA ACT TCT GCT GCT  Met Leu Asn Ile Leu Lys Thr Leu Thr Ser Ala Ala  -10  -5	110
CTT CCC TCC CCC CCC CGC CCC AAC AAG AGG Leu Pro Ser Pro Arg Pro Asn Lys Arg  1 5	143
(2) INFORMATION FOR SEQ ID NO: 150:	
<ul> <li>(i) SEQUENCE CHARACTERISTICS:</li> <li>(A) LENGTH: 176 base pairs</li> <li>(B) TYPE: NUCLEIC ACID</li> <li>(C) STRANDEDNESS: DOUBLE</li> <li>(D) TOPOLOGY: LINEAR</li> </ul>	
(ii) MOLECULE TYPE: CDNA	
<pre>(vi) ORIGINAL SOURCE:     (A) ORGANISM: Homo Sapiens     (F) TISSUE TYPE: Brain</pre>	
(ix) FEATURE:  (A) NAME/KEY: sig_peptide  (B) LOCATION: 24143  (C) IDENTIFICATION METHOD: Von Heijne matrix  (D) OTHER INFORMATION: score 3.9  seq SPLLCLYHPPYYT/ST	

seq SPLLCLYHPPVYT/ST

( $\mbox{\em 11}$ ) SEQUENCE DESCRIPTION: SEQ ID NO: 150:

116	
AGTAATCCCA GGCGTTCGCC CTC ATG CGG GCC AGG GTT TGG CCT CGC TCC CAC  Met Arg Ala Arg Val Trp Pro Arg Ser His  -40  -35	53
GGG ATC CCT GTG CCT TCC TTT CTC TCT AAG AGC AGC CTC AGT CAT ACA Gly Ile Pro Val Pro Ser Phe Leu Ser Lys Ser Ser Leu Ser His Thr -30 -25 -20 -15	101
CCA TCA CCT CTC CTC TGT CTA TAC CAT CCT CCT GTC TAC ACC AGC ACC Pro Ser Pro Leu Leu Cys Leu Tyr His Pro Pro Val Tyr Thr Ser Thr -10 -5 1	149
ACT ACC CCA TCT ATA CCA CCA CGT CTG Thr Thr Pro Ser Ile Pro Pro Arg Leu 5 10	176
(2) INFORMATION FOR SEQ ID NO: 151:	
(i) SEQUENCE CHARACTERISTICS:  (A) LENGTH: 414 base pairs  (B) TYPE: NUCLEIC ACID  (C) STRANDEDNESS: DOUBLE  (D) TOPOLOGY: LINEAR	
(ii) MOLECULE TYPE: CDNA	
<pre>(vi) ORIGINAL SOURCE:     (A) ORGANISM: Homo Sapiens     (F) TISSUE TYPE: Brain</pre>	
<pre>(ix) FEATURE:     (A) NAME/KEY: sig_peptide     (3) LOCATION: 262369     (C) IDENTIFICATION METHOD: Von Heijne matrix     (D) OTHER INFORMATION: score 3.9</pre>	
(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 151:	
AAAGTAGGAA ATGGCTGCTT CACCCAGGAG GCACCAAGAT GCCCGTGTGT GGCTCTACTG	60
GTGATGCCCT GGTCTTCATT GAAAAGGCCA GCACCCGTTA CGTGGTCAGC ACAGACGTTG	120
CCGTGAATGA GGATTCCTTC CTACAGATAG ACTTCGCTGC CTCCTGCTCA GTCACAGACT	180
CTTGTTATGC GATTGAATTG GAATACTCAG TAGATCTTGG ATTGTCATGG CACCCATTGG	240
TAAGGGACTG TCTGCCTACC A ATG TGG AAT GCA GTC GCT ATC ATC TGC AAC  Met Trp Asn Ala Val Ala Ile Ile Cys Asn  -35	291
GGA TCC TGG TGT CAG ACA CDW TCA ACA AGT GGA CTA GAA TCA CTC TGC Gly Ser Trp Cys Gln Thr Xaa Ser Thr Ser Gly Leu Glu Ser Leu Cys -25 -20 -15	339
CTC TCC CTC CTT ATA CCA GGT CCC AAG CCA CTC GTT TCC GTT GGC ATC Leu Ser Leu Leu Ile Pro Gly Pro Lys Pro Leu Val Ser Val Gly Ile -10 -5 1 5	387

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 152:

AAAAATTATT TCTGCTTAAA CAACAGTTTC AAATATTTCT CTTTTGAAGA CAAAATTGGT 60

TTAGTTTCAG CAATGTATTG ATATAATTTT ACATTTTTTT AA ATG TTG AGG CTG Met Leu Arg Leu

GGT TTA TTT AAG ATT AGC TGG GCT CGC TGC CTA TCA TAT AGT AAA ACC 162
Gly Leu Phe Lys Ile Ser Trp Ala Arg Cys Leu Ser Tyr Ser Lys Thr -10 -5 1 5

CAG CBC GAA 171
Gln Xaa Glu

(C) IDENTIFICATION METHOD: Von Heijne matrix

seq LRLGLFKISWARC/LS

(D) OTHER INFORMATION: score 3.9

#### (2) INFORMATION FOR SEQ ID NO: 153:

- (i) SEQUENCE CHARACTERISTICS:
  - (A) LENGTH: 262 base pairs
  - (B) TYPE: NUCLEIC ACID
  - (C) STRANDEDNESS: DOUBLE
  - (D) TOPOLOGY: LINEAR
- (ii) MOLECULE TYPE: CDNA
- (vi) ORIGINAL SOURCE:
  - (A) ORGANISM: Homo Sapiens
  - (F) TISSUE TYPE: Brain
- (ix) FEATURE:
  - (A) NAME/KEY: sig\_peptide

(B) LOCATION: 80..187

118

(C) IDENTIFICATION METHOD: Von Heijne matrix (D) OTHER INFORMATION: score 3.9 seq VVEILPYLPCLTA/RD	
(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 153:	
AGGGGTACCG AGTCTCGTTT CCTCTCAGTC CATCCACCCT TCATGGGGCC AGAGCCCTCT	60
CTCCAGAATC TGAGCAGCA ATG CCG TTT GCT GAA GAC AAG ACC TAT AAG TAT  Met Pro Phe Ala Glu Asp Lys Thr Tyr Lys Tyr  -35 -30	112
ATC TGC CGC AAT TTC AGC AAT TTT TGC AAT GTG GAT GTT GTA GAG ATT Ile Cys Arg Asn Phe Ser Asn Phe Cys Asn Val Asp Val Val Glu Ile -25 -10	160
CTG CCT TAC CTG CCC TGC CTC ACA GCA AGA GAC CAG GAT CGA CTG CGG Leu Pro Tyr Leu Pro Cys Leu Thr Ala Arg Asp Gln Asp Arg Leu Arg -5 1 5	208
GCC ACC TGC ACA CTC TCA GGG AAC CGG GAC ACC CTC TGG CAT CTC TTC Ala Thr Cys Thr Leu Ser Gly Asn Arg Asp Thr Leu Trp His Leu Phe 10 15 20	256
AAT ACC Asn Thr 25	262
(2) INFORMATION FOR SEQ ID NO: 154:  (i) SEQUENCE CHARACTERISTICS:  (A) LENGTH: 165 base pairs  (B) TYPE: NUCLEIC ACID  (C) STRANDEDNESS: DOUBLE  (D) TOPOLOGY: LINEAR  (ii) MOLECULE TYPE: CDNA  (vi) ORIGINAL SOURCE:  (A) ORGANISM: Homo Sapiens  (F) TISSUE TYPE: Brain  (ix) FEATURE:  (A) NAME/KEY: sig_peptide  (B) LOCATION: 46153	
<pre>(C) IDENTIFICATION METHOD: Von Heijne matrix (D) OTHER INFORMATION: score 3.8</pre>	
AATCATGAAA TCCTTGCAAC TCATTAAGTT TCCTGTTTGC TGTAG ATG CCA GGA AGC Met Pro Gly Ser -35	57
TCA GGG CTC AGA TTT ATA TGT AAG TCC AGG AAC CAT CCT CAG TTT GGG	105

ACAT	racgo	GGC A	\AGT1	TAT	AA GC	GTC	STCAT	GTC	CAAAA	ACGG	GCCF	AGCTI	rgc <i>f</i>	AGCCA	ATCAAG	60
GTT						GAT Asp										108
						TCT Ser										156
		Phe				AAC Asn -20										204
						GGT Gly										252
		GGG Gly														261

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 126 base pairs

(C)	TYPE: NUCLEIC ACID STRANDEDNESS: DOUBLE TOPOLOGY: LINEAR	
(ii) MOLEC	ULE TYPE: CDNA	
(A)	NAL SOURCE: ORGANISM: Homo Sapiens TISSUE TYPE: Brain	
(B) (C)	RE: NAME/KEY: sig_peptide LOCATION: 49120 IDENTIFICATION METHOD: Von Heijne matrix OTHER INFORMATION: score 3.8 seq KLFLVFLLNICKG/IV	
(xi) SEQUE	CNCE DESCRIPTION: SEQ ID NO: 156:	
ATCTCTAGAA AGAAG	GAAGGC ATGCTACAAA TAGGAAGGAA TTGTAATA ATG ATA TTT Met Ile Phe	57
GGC CTC TAC TTT Gly Leu Tyr Phe -20	GTC TTA GCT GTT AAA CTG TTT TTA GTA TTT TTG TTA Val Leu Ala Val Lys Leu Phe Leu Val Phe Leu Leu -15 -10	105
AAT ATT TGC AAA Asn Ile Cys Lys -5		126
(i) SEQUEN (A) (B) (C)	FOR SEQ ID NO: 157:  NCE CHARACTERISTICS: LENGTH: 383 base pairs TYPE: NUCLEIC ACID STRANDEDNESS: DOUBLE TOPOLOGY: LINEAR	
(ii) MOLEC	CULE TYPE: CDNA	
(A)	INAL SOURCE: ORGANISM: Homo Sapiens TISSUE TYPE: Brain	
(B) (C)	URE:  NAME/KEY: sig_peptide  LOCATION: 246347  IDENTIFICATION METHOD: Von Heijne matrix  OTHER INFORMATION: score 3.6  seq IKCSSWISSLASG/IP	

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 157:

	00332	121	PCT/IB98/0
TTCAGATC	TT GGGTTCAGGA GCG;	AGACCCA TGTCTGAAAT ATAAACTTGC TCACTGT	Che too
CCTGTGAT	GG TCTTTGTGAG ACAT	PAGAATG AATATTAATA AAGAGGTGTA AGGACTG	CAG 120
CTGGGATC	AT CCACAGTAAG GOTO	CCCCAN CARACTARIA AAGAGGTGTA AGGACTG	ATC 180
GATCC ATC	2 700 770 770	GGGGGAA GAGGAGACCT GGCAAAGGAA TCAAAGA	CAT 240
	-30	GTR GAA GAA CTA ATA GTG TTT CCA GGA (Val Glu Glu Leu Ile Val Phe Pro Gly (-25	Glu -20
	-15	C AAG TGC TCC TCT TGG ATT TCT TCC CTC e Lys Cys Ser Ser Trp Ile Ser Ser Let -10	338
GCT TCT G Ala Ser G	GA ATA CCA CAC TC ly Ile Pro His Se l	T CTT GGA TTC TCC CTT CCC CCA GGG r Leu Gly Phe Ser Leu Pro Pro Gly 5	383
(2) INFOR	MATION FOR SEQ ID	NO: 158:	
(i)	SEQUENCE CHARACTE (A) LENGTH: 427 (B) TYPE: NUCLE (C) STRANDEDNES (D) TOPOLOGY: L	base pairs IC ACID S: DOUBLE	
(ii)	MOLECULE TYPE: C	DNA	
(vi)	ORIGINAL SOURCE: (A) ORGANISM: H (F) TISSUE TYPE	omo Sapiens : Brain	
(ix)	FEATURE: (A) NAME/KEY: s: (B) LOCATION: 2! (C) IDENTIFICAT: (D) OTHER INFORM	57340 ION METHOD: Von Hoise	
(xi)	SEQUENCE DESCRIPT	FION: SEQ ID NO: 158:	
AAGAACCCTT	TTTATAGATA GGTCTT	IGTCT GGATTTGTGC ACGTGGATTT ATAATGAGA	G 60
ATTTTCTAGT	TGTTTTTGGT TCTCCT	CCCTC CTCCTCCTCC TTTDHCCTCC TTCTVTTCC	т 120
CCTTTTCTTC	CTCCTTWTCT TCTAAF	AACCT CTAATCTCTT ATTCCCTCTA ATGTCTGAC	T 120
AAAGTACTGC	TGTCTGAGAC ATTGGA	AGGCA TACTGTGCTC CTCTTCTTCC CTCCCTGTG	C 180
AGAAGCCTTA	AGTTAT ATG CCT TO	CA TCC AGT CTT GCA GAG TTG TGT CTA ATC er Ser Ser Leu Ala Glu Leu Cys Leu Met -25	

-25

CAG CAA GAT GCC TGC CTG TTT TCT KTG TTC CTA GCW GTC TCC AGG CAT
Gln Gln Asp Ala Cys Leu Phe Ser Xaa Phe Leu Ala Val Ser Arg His
-15
-10
-10
-15

-20

CCA AAC TAT NVK TGT TCC ATC AGT ACT AAG GGT GAG GTG AGA GAG AAA

Pro Asn Tyr Xaa Cys Ser Ile Ser Thr Lys Gly Glu Val Arg Glu Lys

1 10 15

CTA GTT CCT TGG ATA ACA CAC CAA ATG GCC AGA ATG TTG
Leu Val Pro Trp Ile Thr His Gln Met Ala Arg Met Leu
20 25

#### (2) INFORMATION FOR SEQ ID NO: 159:

- (i) SEQUENCE CHARACTERISTICS:
  - (A) LENGTH: 158 base pairs
  - (B) TYPE: NUCLEIC ACID
  - (C) STRANDEDNESS: DOUBLE
  - (D) TOPOLOGY: LINEAR
- (ii) MOLECULE TYPE: CDNA
- (vi) ORIGINAL SOURCE:
  - (A) ORGANISM: Homo Sapiens
  - (F) TISSUE TYPE: Brain
- (ix) FEATURE:
  - (A) NAME/KEY: sig\_peptide
  - (B) LOCATION: 21..140
  - (C) IDENTIFICATION METHOD: Von Heijne matrix
  - (D) OTHER INFORMATION: score 3.6

seq LQMRMQLPCLVLG/EE

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 159:

AATTITCAGT AGGAAACATT ATG GAT CTG TGG AGC TGC TTA TTT CCA GTG ATG

Met Asp Leu Trp Ser Cys Leu Phe Pro Val Met

-40

-35

-30

CTG ATG GAG CCA TCC AAA GGG CTG GAA GAT TCA GAG TGG AAA ATG GCT

Leu Met Glu Pro Ser Lys Gly Leu Glu Asp Ser Glu Trp Lys Met Ala

-25

-20

-15

CTT CAG ATG AGA ATG CAA CTG CCC TGC CTG GTA CTT GGC GAA GAA CAG
Leu Gln Met Arg Met Gln Leu Pro Cys Leu Val Leu Gly Glu Glu Gln
-10 -5

ACG CTT GGG
Thr Leu Gly

# (2) INFORMATION FOR SEQ ID NO: 160:

- (i) SEQUENCE CHARACTERISTICS:
  - (A) LENGTH: 319 base pairs
  - (B) TYPE: NUCLEIC ACID
  - (C) STRANDEDNESS: DOUBLE
  - (D) TOPOLOGY: LINEAR
- (ii) MOLECULE TYPE: CDNA

123

(vi)	ORIGINAL SOURCE: (A) ORGANISM: Homo Sapiens (F) TISSUE TYPE: Brain	
(ix)	FEATURE:  (A) NAME/KEY: sig_peptide  (B) LOCATION: 209289  (C) IDENTIFICATION METHOD: Von Heijne matrix  (D) OTHER INFORMATION: score 3.6  seq AVPLPTTSTLTSA/ST	
(xi)	SEQUENCE DESCRIPTION: SEQ ID NO: 160:	
AAGTTCTGTG	GGCTCTATTC GGCCATATTA ATAAAGAGAA AGGGAAGGCT GACHGTCCTT	60
CGCCTCCGCC	CCCACATACA CACCCCTTCT TCCCACTCCG CTCTCACGAC TAAGCTCTCA	120
CGATTAAGGC	ACGCCTGCCT CGATTGTCCA GCCTCTGCCA GAAGAAAGCT TAGCAGCCAG	180
CGCCTCAGTA	GAGACCTAAG GGCGCTGA ATG AGT GGG AAA GGG AAA TGC CGA Met Ser Gly Lys Gly Lys Cys Arg -25 -20	232
	CG CTG CGG CGG GCT GTG CCA TTA CCT ACA ACA AGC ACA TTA  La Leu Arg Arg Ala Val Pro Leu Pro Thr Thr Ser Thr Leu  -15 -5	280
	CT TCC ACA GGT TTC CTT TGG ATC CTA AAA GAA .a Ser Thr Gly Phe Leu Trp Ile Leu Lys Glu 1 5 10	319
(2) INFORM	MATION FOR SEQ ID NO: 161:	
(i)	SEQUENCE CHARACTERISTICS:  (A) LENGTH: 91 base pairs  (B) TYPE: NUCLEIC ACID  (C) STRANDEDNESS: DOUBLE  (D) TOPOLOGY: LINEAR	
(ii)	MOLECULE TYPE: CDNA	
(vi)	ORIGINAL SOURCE: (A) ORGANISM: Homo Sapiens (F) TISSUE TYPE: Brain	
(ix)	FEATURE:	

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 161:

(D) OTHER INFORMATION: score 3.6

(A) NAME/KEY: sig\_peptide (B) LOCATION: 14..67

(C) IDENTIFICATION METHOD: Von Heijne matrix

seq IOKSSGLFCPSQA/QS

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-15 -10 TTC TGC CCA TCA CAG GCC CAG AGC GCA AGA CCC GCA GAA AAG 91 Phe Cys Pro Ser Gln Ala Gln Ser Ala Arg Pro Ala Glu Lys (2) INFORMATION FOR SEQ ID NO: 162: (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 364 base pairs (B) TYPE: NUCLEIC ACID (C) STRANDEDNESS: DOUBLE (D) TOPOLOGY: LINEAR (ii) MOLECULE TYPE: CDNA (vi) ORIGINAL SOURCE: (A) ORGANISM: Homo Sapiens (F) TISSUE TYPE: Brain (ix) FEATURE: (A) NAME/KEY: sig\_peptide (B) LOCATION: 56..271 (C) IDENTIFICATION METHOD: Von Heijne matrix (D) OTHER INFORMATION: score 3.6 seq CTSLLQLYDASNS/EW (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 162: AAACTCGCTG GGCTCCAAAA GAAACACTGG CTTCTCTCCT TCAGCTCCAG GCTAG ATG 58 Met CCA GAC CAG TTT GAC CAG GCG GTT GTG CTG AAC CAG CTG CGG TAC TCA 106 Pro Asp Gln Phe Asp Gln Ala Val Leu Asn Gln Leu Arg Tyr Ser -65 GGG ATG CTG GAG ACT GTG AGA ATC CGC AAA GCT GGG TAT GCG GTC CGA 154 Gly Met Leu Glu Thr Val Arg Ile Arg Lys Ala Gly Tyr Ala Val Arg AGA CCC TTT CAG GAC TTT TAC AAA AGG TAT AAA GTG CTG ATG AGG AAT 202 Arg Pro Phe Gln Asp Phe Tyr Lys Arg Tyr Lys Val Leu Met Arg Asn -35CTG GCT CTG CCT GAG GAC GTC CGA GGG AAG TGC ACG AGC CTG CTG CAG 250 Leu Ala Leu Pro Glu Asp Val Arg Gly Lys Cys Thr Ser Leu Leu Gln CTC TAT GAT GCC TCC AAC AGC GAG TGG CAG CTG GGG AAG ACC AAG GTC 298 Leu Tyr Asp Ala Ser Asn Ser Glu Trp Gln Leu Gly Lys Thr Lys Val -5 TTT CTT CGA GAA TCC TTG GAA CAG AAA CTG GAG AAG CGG AGG GAA GAG Phe Leu Arg Glu Ser Leu Glu Gln Lys Leu Glu Lys Arg Arg Glu Glu 15 20

364

GAA GTG AGC CAC GCT GGG

Glu Val Ser His Ala Gly

PCT/IB98/01236 125

(2) INFORMATION FOR SEQ ID NO: 163:	
<ul> <li>(i) SEQUENCE CHARACTERISTICS:</li> <li>(A) LENGTH: 185 base pairs</li> <li>(B) TYPE: NUCLEIC ACID</li> <li>(C) STRANDEDNESS: DOUBLE</li> <li>(D) TOPOLOGY: LINEAR</li> </ul>	
(ii) MOLECULE TYPE: CDNA	
<pre>(vi) ORIGINAL SOURCE:     (A) ORGANISM: Homo Sapiens     (F) TISSUE TYPE: Brain</pre>	
<pre>(ix) FEATURE:     (A) NAME/KEY: sig_peptide     (B) LOCATION: 129173     (C) IDENTIFICATION METHOD: Von Heijne matrix     (D) OTHER INFORMATION: score 3.6</pre>	
(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 163:	
AGTAGACCGC GCACTGGAAG GCGTGCGCGC AGGTGTGCGT GACCATGTGC TTGAAACGGC	60
AGTAGCGCAS RNGNAAGGAT CGCCATCACA CGGCGCACTG GTGCGGCTTC TCCCCCGAGT	120
GGACGAAC ATG TGC TTG GTG TCG TTT TTC CTT GAG CTG AAC GTC TTG CAA  Met Cys Leu Val Ser Phe Phe Leu Glu Leu Asn Val Leu Gln  -15	170
CAG TGG CCG GCA GGG Gln Trp Pro Ala Gly 1	185
(2) INFORMATION FOR SEQ ID NO: 164:	
(i) SEQUENCE CHARACTERISTICS:  (A) LENGTH: 234 base pains	

# (2

- (B) TYPE: NUCLEIC ACID
- (C) STRANDEDNESS: DOUBLE
  (D) TOPOLOGY: LINEAR
- (ii) MOLECULE TYPE: CDNA
- (vi) ORIGINAL SOURCE:
  - (A) ORGANISM: Homo Sapiens
    (F) TISSUE TYPE: Brain
- (ix) FEATURE:
  - (A) NAME/KEY: sig\_peptide
    (B) LOCATION: 103..141

  - (C) IDENTIFICATION METHOD: Von Heijne matrix
  - (D) OTHER INFORMATION: score 3.6

seq MRSLACLTPCGHA/GS

#### xi) SEQUENCE DESCRIPTION: SEQ ID NO: 164:

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 164:	
ATACCTCTTC CAGTTGGGAA AAAATGGACT TAAAATGTCC CATGTCCAGG CTGACCTGGA	60
TGATGACAGT TGGTTGATGA GTTAATTTGA ACATGAGCAG AA ATG AGG TCA CTT Met Arg Ser Leu -10	114
GCC TGC CTG ACT CCA TGT GGC CAT GCT GGC TCC AGG TTG CAA AGT TCT Ala Cys Leu Thr Pro Cys Gly His Ala Gly Ser Arg Leu Gln Ser Ser -5 1 5	162
TTG AGC AAG TAC CTT GTC TTG CCT AAT CTC GAA TGT CTG TTC TTT TTA Leu Ser Lys Tyr Leu Val Leu Pro Asn Leu Glu Cys Leu Phe Phe Leu 10 15 20	210
TTT CTT ATC TCA AAT AGG CGC TGG Phe Leu Ile Ser Asn Arg Arg Trp 25 30	234
(2) INFORMATION FOR SEQ ID NO: 165:  (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 315 base pairs (B) TYPE: NUCLEIC ACID (C) STRANDEDNESS: DOUBLE (D) TOPOLOGY: LINEAR  (ii) MOLECULE TYPE: CDNA  (vi) ORIGINAL SOURCE: (A) ORGANISM: Homo Sapiens (F) TISSUE TYPE: Brain  (ix) FEATURE: (A) NAME/KEY: sig_peptide (B) LOCATION: 70108 (C) IDENTIFICATION METHOD: Von Heijne matrix (D) OTHER INFORMATION: score 3.5 seq MHLLSNWANPASS/RR  (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 165:	
AAGTGGCCAT GGCGGATACA GCGACTACAG CATCGGCGGC GGCGGCTAGT GCCGCTAGCG	60
CCTCGAGCG ATG CAC CTC CTT TCC AAC TGG GCA AAC CCC GCT TCC AGC AGA  Met His Leu Leu Ser Asn Trp Ala Asn Pro Ala Ser Ser Arg  -10  -5  1	111
CGT CCT TCT ATG GCC GCT TCA GGC ACT TCT TGG ATA TCA TCG ACC CTC Arg Pro Ser Met Ala Ala Ser Gly Thr Ser Trp Ile Ser Ser Thr Leu 5 10 15	159

GCA CAC TCT TTG TCA CTG AGA GAC GTC TCA GAG AGG CTG TGC AGC TGC
Ala His Ser Leu Ser Leu Arg Asp Val Ser Glu Arg Leu Cys Ser Cys

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20		25	127		1 0 1/10/0/01230
TGG AGG ACT ATA	NCO			30	
TGG AGG ACT ATA Trp Arg Thr Ile 35	Ser Met Gly	rro cys i	GCC CGG GGG Ala Arg Gly 45	TCA CCA ATG AAC Ser Pro Met Asn	255
AGC TCT GGA GTG Ser Ser Gly Val 50	CAC AGA AAA His Arg Lys 55	TCA AGC A	AGG CTA TTC Arg Leu Phe 60	TAC ATC CGG ACA Tyr Ile Arg Thr 65	303
CCA ATG AGA AGA Pro Met Arg Arg					315
(A) I (B) T (C) S	FOR SEQ ID ID ICE CHARACTER LENGTH: 415 TYPE: NUCLEIE STRANDEDNESS TOPOLOGY: LI	RISTICS: base pair: C ACID	s		
	JLE TYPE: CD				
(vi) ORIGIN (A) O (F) T	NAL SOURCE: PRGANISM: Ho 'ISSUE TYPE:	mo Sapiens Brain	s		
(C) I	AME/KEY: si OCATION: 62	133 On method: Ation: sc	: Von Heijne core 3.5 :q FAMLHSVWR:		
(xi) SEQUEN	CE DESCRIPT			DIFA/ER	
AAAGGAGCCA ACYKCA	CAGT ACATTT	CTCT TTGTC	TATCAA TTCCA		
C ATG TGG TCT GGA	AAG TGC CC	* ****C C#*			
- · · · · · · · · · · · · · · · · · · ·	-20 TEP AL	a ren Aal	-15	Ala Met Leu His	109
TCA GTG TGG AGA C Ser Val Trp Arg Le -5		l l	g GIY TYP A	La Gln Gln Asp 5	157
GCT CAG GAA TTT CT Ala Gln Glu Phe Le 10	15	sed bed As	p Lys IIe G1 20	ln Arg Glu Leu	205
GAG ACA ACT GGT AC Glu Thr Thr Gly Th 25	30	to Ala Le	u lle Pro Th 35	er Ser Gln Arg 40	253
AAA CTC ATC AAA CF Lys Leu Ile Lys Gl 4	AA GTT CTG # In Val Leu # 15	AT GTT GTA Asn Val Va 50	ı Asn Asn Il	TT TTT CAT GGA e Phe His Gly 55	301

., .		_						128	3						
CAA CTI Gln Leu															349
ACC ATA															397
CAA TGC Gln Cys 90	Ser														415
	ORMA  (i) S  (ii) (vi) (ix)	EQUENCE (A) (B) (C) (A) (F) FEAT (A) (B) (C) (D)	NCE OLENGTYPE STRATOPO CULE INAL ORGA TISS URE: NAME LOCA IDEN OTHE	CHARACTH: C: NU ANDED DLOGY TYPE SOUR ANISM E/KEY ATION OTIFICER IN	CTEFE 252 CCLEI CCLEI CNESS C: LI CE: CI CRCE: C	base C AC C: DC C: DC C: NEAH DNA DMO S C: Bra C: Bra C: MATIC	ICS: pai CID OUBLE R Sapi ain epti METHO ON:	ens de DD: '	re 3 KFC	.5 LICL	LTFI				
AAGACG	CGCC	GGTT	TCTG	CG A	CGCA	GTTA	.G CG	CAGT	CTGC	TTT	GGTG	TAA	ACAC	GATTT(	G 60
GTGCAG	CCGG	GGTT	TGGT.	AC C	GAGC	GGAG	A GG	AGAT	GCAC	ACG	GCAC	TCG	AGTG	TGAGG	A 120
AAAATA	ŀ					et H					ys I			GT TTO Cys Le	
CTG AC Leu Th						Cys				His					219
CAT GG His Gl				Leu					Gly						252
(2) IN	FORM	ATIO	1 FOF	R SEC	O ID	NO:	168:	:							
	(i) :		ENCE LEN TYP	IGTH:	436	bas	se pa								

129	
(C) STRANDEDNESS: DOUBLE (D) TOPOLOGY: LINEAR	
(ii) MOLECULE TYPE: CDNA	
<pre>(vi) ORIGINAL SOURCE:     (A) ORGANISM: Homo Sapiens     (F) TISSUE TYPE: Brain</pre>	
<pre>(ix) FEATURE:</pre>	
(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 168:	
ATATTTCTTG TCAACAGTAT TGAAATGTAA TATGTATGTG TTCATGTATG AGMAATTTT	T 60
ACTCCACACA GGTGTTTCAG TAGAGTGGGG CAGGAAAAGA GATCTCTTCG ATTTCTTTC	A 120
GGCCTGAGGC TTTTGTGAAA TGCGTCASCC CCTGTGACAG TAGGTTTTGA TGCTAGTGA	T 180
CTTCAGATCT TTCTCTCTGG AAATGTGCAG AGAGTGTCAG TTTCCCAAGT TCTGAGGTA	240
CTCTCAGCCC AGATGTGAAA TGGGAGCCTA CCAGCTGGTA TAGAAGGGA ATG GGT AG Met Gly Ard	G 298
AGG CAC TGG GTG CTG ACT CAT TCA GCA CTG TCC CTT TTC TAT ACT GCT Arg His Trp Val Leu Thr His Ser Ala Leu Ser Leu Phe Tyr Thr Ala -10	346
GAT ACA TCC CAT GGT TCT GAG AAG CCT TAT CTC AGT CTA TTT GGA AGA Asp Thr Ser His Gly Ser Glu Lys Pro Tyr Leu Ser Leu Phe Gly Arg 1 5 10	394
GAG GGA GGW AGA GAA GGR AGT AAC CCA AAG TAC TAC TCA TTT Glu Gly Gly Arg Glu Gly Ser Asn Pro Lys Tyr Tyr Ser Phe 15 20 25	436
(2) INFORMATION FOR SEQ ID NO: 169:	
(i) SEQUENCE CHARACTERISTICS:  (A) LENGTH: 343 base pairs  (B) TYPE: NUCLEIC ACID  (C) STRANDEDNESS: DOUBLE  (D) TOPOLOGY: LINEAR	
(ii) MOLECULE TYPE: CDNA	
<ul><li>(vi) ORIGINAL SOURCE:</li><li>(A) ORGANISM: Homo Sapiens</li><li>(F) TISSUE TYPE: Brain</li></ul>	
(ix) FEATURE:	

(A) NAME/KEY: other
(B) LOCATION: 104..336

WO 99/06552 130 (C) IDENTIFICATION METHOD: blastn (D) OTHER INFORMATION: identity 96 region 1..233 id H07998 est (ix) FEATURE: (A) NAME/KEY: other (B) LOCATION: 110..336 (C) IDENTIFICATION METHOD: blastn (D) OTHER INFORMATION: identity 96 region 1..227 id W37530 est (ix) FEATURE: (A) NAME/KEY: other (B) LOCATION: 110..336 (C) IDENTIFICATION METHOD: blastn (D) OTHER INFORMATION: identity 96 region 1..227 id R79812 est (ix) FEATURE: (A) NAME/KEY: other (B) LOCATION: 110..336 (C) IDENTIFICATION METHOD: blastn (D) OTHER INFORMATION: identity 96 region 1..227 id N24900 est (ix) FEATURE: (A) NAME/KEY: other (B) LOCATION: 110..336 (C) IDENTIFICATION METHOD: blastn (D) OTHER INFORMATION: identity 96 region 1..227 id R34849 (ix) FEATURE: (A) NAME/KEY: sig\_peptide (B) LOCATION: 65..112 (C) IDENTIFICATION METHOD: Von Heijne matrix (D) OTHER INFORMATION: score 12.5 seq FVVLLALVAGVLG/NE (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 169: ATGTCGCCCG TGTCCCGCCG GCCCGTTCCG TGTCGCCCCG CAGTGYTGCG GCCGCCGCKK 60 109 Met Ala Val Phe Val Val Leu Leu Ala Leu Val Ala Gly Val Leu

-10

GGG AAC GAG TTT AGT ATA TTA AAA TCA CCA GGG TCT GTT GTT TTC CGA

Gly Asn Glu Phe Ser Ile Leu Lys Ser Pro Gly Ser Val Val Phe Arg

10

157

-15

AAT GGA AAT TGG CCT ATA CCA GGA GAG CGG ATC CCA GAC GTG GCT GCA ASN Gly Asn Trp Pro 11e Pro Gly Glu Arg 11e Pro Asp Val Ala Ala 30

TTG TCC ATG GGC TTC TCT GTG AAA GAA GAC CTT TCT TGT GGG CCA GGA CTC Leu Ser Met Gly Phe Ser Val Lys Glu Asp Leu 45

GCA GTG GGT AAC CTG TTT CAT CGT CCT ASP Val Asp Asn Asn Asn Xaa Pro Leu Pro Pro Xaa Trp Xaa

GTG AAG GGA GTT AAC AAC TMC CCT CTA CCC CCA NGN TGG NGG ATG A43

A343

# (2) INFORMATION FOR SEQ ID NO: 170:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 234 base pairs

(B) TYPE: NUCLEIC ACID

(C) STRANDEDNESS: DOUBLE

(D) TOPOLOGY: LINEAR

- (ii) MOLECULE TYPE: CDNA
- (vi) ORIGINAL SOURCE:
  - (A) ORGANISM: Homo Sapiens
  - (F) TISSUE TYPE: Brain
- (ix) FEATURE:
  - (A) NAME/KEY: other
  - (B) LOCATION: 111..209
  - (C) IDENTIFICATION METHOD: blastn
  - (D) OTHER INFORMATION: identity 90 region 1..99

id N50844

est

- (ix) FEATURE:
  - (A) NAME/KEY: other
  - (B) LOCATION: 186..232
  - (C) IDENTIFICATION METHOD: blastn
  - (D) OTHER INFORMATION: identity 93

region 75..121 id N50844

est

- (ix) FEATURE:
  - (A) NAME/KEY: other
  - (B) LOCATION: 111..209
  - (C) IDENTIFICATION METHOD: blastn
  - (D) OTHER INFORMATION: identity 90

region 1..99

id N29905

est

(ix) FEATURE:

WO 99/06552		132	1	PCT/IB98/0
(B) (C)	NAME/KEY: other LOCATION: 186232 IDENTIFICATION METHO OTHER INFORMATION:	DD: blastn identity 93 region 75l id N29905 est	21	
(B) (C)	URE: NAME/KEY: other LOCATION: 186232 IDENTIFICATION METHO OTHER INFORMATION:	DD: blastn identity 93 region 751 id N62597 est	.21	
(B) (C)	URE: NAME/KEY: other LOCATION: 186232 IDENTIFICATION METHO OTHER INFORMATION:		122	
(B) (C)	URE: NAME/KEY: other LOCATION: 186232 IDENTIFICATION METHO OTHER INFORMATION:		122	
(B) (C)	URE: NAME/KEY: sig_pepti LOCATION: 4087 IDENTIFICATION METH OTHER INFORMATION:			
(xi) SEQU	ENCE DESCRIPTION: SE	Q ID NO: 170	:	
AAGAGGTGCG GGAT	TTGGGCG GGCTGCCACG GC		GCT CCG CTT CT Ala Pro Leu Le -15	
	G GTG CTC GGC GCG GCG			

CTG ATT TCC ATC GTT GCA TTT ACA ACT GCT ACA AAA ATG CCA GCA CTC

Lew Ile Ser Ile Val Ala Phe Thr Thr Ala Thr Lys Met Pro Ala Leu

CAT CGA CAT GAA GAA GAG AAA TTC TTC TTA AAT GCC AAA GGC CAG AAA

His Arg His Glu Glu Glu Lys Phe Phe Leu Asn Ala Lys Gly Gln Lys

-10

WO 99/06552 PCT/IB98/01236

***************************************	133	
GAA ACT TTA CCC Glu Thr Leu Pro 40	AGU ATA TGG GAC TUA CCT ACC AGG Ser lie Trp Asp der Pro Thr Arg 45	234
(2) INFORMATION	FOR SEQ ID NO: 171:	
(A) (B) (C)	NCE CHARACTERISTICS: LENGTH: 386 base pairs TYPE: NUCLEIC ACID STRANDEDNESS: DOUBLE TOPOLOGY: LINEAR	
(ii) MOLE	CULE TYPE: CDNA	
(A)	INAL SOURCE: ORGANISM: Homo Sapiens TISSUE TYPE: Brain	
(B) (C)	URE:  NAME/KEY: other  LOCATION: 52228  IDENTIFICATION METHOD: blastn  OTHER INFORMATION: identity 94  region 1177  id AA074050  est	
(B) (C)	URE:  NAME/KEY: other  LOCATION: 266387  IDENTIFICATION METHOD: blastn  OTHER INFORMATION: identity 99  region 218339  id AA074050  est	
(B) (C)	NURE:  NAME/KEY: sig_peptide  LOCATION: 135284  IDENTIFICATION METHOD: Von Heijne matrix  OTHER INFORMATION: score 9.8  seq_LLRLLQLVSTCVA/FS	
(xi) SEQU	JENCE DESCRIPTION: SEQ ID NO: 171:	
AGCGGCCCA GCC	AGCCAGG CCGCGCMMGG GACGACTGCA GAGCGCGGTG CTCTTACAGC	60
THITTOCAAG TGT	GSCTTAA TCCGTCTCCA CCACCAGATC TTTCTCCGTG GATTCCTCTC	120
UTAAGACCGC TGCC	E ATO CCA GTG ACG GTA ACC CGC ACC ACC ATC ACA ACC Met Pro Val Thr Val Thr Arg Thr Thr fle Thr Thr -50 -40	170
	A TOT TOG GGC CTG GGG TCC CCC ATG ATC GTG GGG TCC r 5%. Ser Gly Leu Gly Ser Pro Met Ile Val Gly Ser -30 -25	219

TIT CGG GCC CTG ATW AWA COO CTG GGT CTC CTT CGC CTG CTG CAG CTG  $\sim 256$ 

Pro Arg Ala Leu Thr Gln Pro Leu Gly Leu Leu Arg Leu Leu Gln Leu

20 -15

GTG TCT ACC TGC GTG GCC TTC TCG CTG GTG GCT AGC GTG GGC GCC TGG

Val Ser Thr Cys Val Ala Phe Ser Leu Val Ala Ser Val Gly Ala Trp

-5 1 5 10

ACG GGG TCC ATG GGC AAC TGG TCC ATG TTC ACC TGG TGC TTC TGC TTC

Thr Gly Ser Met Gly Asn Trp Ser Met Phe Thr Trp Cys Phe Cys Phe

15 20 25

TCN GTG ACC CTG ATC ATC CTC ATC
Ser Val Thr Leu Ile Leu Ile
30

386

#### (2) INFORMATION FOR SEQ ID NO: 172:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 326 base pairs

(B) TYPE: NUCLEIC ACID

(C) STRANDEDNESS: DOUBLE

(D) TOPOLOGY: LINEAR

#### (ii) MOLECULE TYPE: CDNA

(vi) ORIGINAL SOURCE:

(A) ORGANISM: Homo Sapiens

(F) TISSUE TYPE: Brain

# (ix) FEATURE:

(A) NAME/KEY: other

(3) LOCATION: 147..290

(C) IDENTIFICATION METHOD: blastn

(D) OTHER INFORMATION: identity 99 region 57..200 id W40499

est

#### (ix) FEATURE:

(A) NAME/KEY: other

(B) LOCATION: 90..151

(C) IDENTIFICATION METHOD: blastn

(D) OTHER INFORMATION: identity 98 region 1..62

id W40499

est

# (ix) FEATURE:

(A) NAME/KEY: other

(B) LOCATION: 100..319

(C) IDENTIFICATION METHOD: blastn

(D) OTHER INFORMATION: identity 99

region 46..265

id R88049

est

#### (ix) FEATURE:

(A) NAME/KEY: other

(B) LOCATION: 100..319

WO 99/06552 135 PCT/IB98/01236

(C) IDENTIFICATION METHOD: blastn (D) OTHER INFORMATION: identity 99 region 56..275 id T08712 est (ix) FEATURE: (A) NAME/KEY: other (B) LOCATION: 100..319 (C) IDENTIFICATION METHOD: blastn (D) OTHER INFORMATION: identity 99 region 32..251 id H38484 (ix) FEATURE: (A) NAME/KEY: other (B) LOCATION: 147..319 (C) IDENTIFICATION METHOD: blastn (D) OTHER INFORMATION: identity 98 region 65..237 id T65344 est (ix) FEATURE: (A) NAME/KEY: other (B) LOCATION: 102..151 (C) IDENTIFICATION METHOD: blastn (D) OTHER INFORMATION: identity 100 region 21..70 id T65344 est (ix) FEATURE: (A) NAME/KEY: sig\_peptide (B) LOCATION: 111..164 (C) IDENTIFICATION METHOD: Von Heijne matrix (D) OTHER INFORMATION: score 9.2 seq VFLCSLLAPMVLA/SA (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 172: AGACTCTTGG GGACTGGGCT GAGGACGGGG TGGTACTGCT CCTGGCAGGG CCAGAGGTGG 60 ATGGGGCTTG ANAMGGGGGT TCAAGGCAGC AGMTCTATGG TTCAGACGCC ATG GAG 116 Met Glu TTG GTG CTG GTC TTC CTC TGC AGC CTG CTG GCC CCC ATG GTC CTG GCC Leu Val Leu Val Phe Leu Cys Ser Leu Leu Ala Pro Met Val Leu Ala 164 -10 AGT GCA GCT GAA AAG GAG AAG GAA ATG GAC CCT TTT CAT TAT GAT TAC Ser Ala Ala Giu Lys Glu Lys Glu Met Asp Pro Phe His Tyr Asp Tyr 212 1.0 CAG ACC CTG AGR ATT GGG GGA CTG GTG TTC GCT GTG GTC CTC TTC TCG Sin Thr Leu Arg Tie Gly Gly Leu Val Phe Ala Val Val Leu Phe Ser 260 25 GTT GGG ATC CTT CTT ATC CTA AGT CGC AGG TGC AAG TGC AGT TTC AAT 309

Val Gly Ile Leu Leu Ile Leu Ser Arg Arg Cys Lys Cys Ser Phe Asn

CAG AAG CCC CGC AAC AGA
Gln Lys Pro Arg Asn Arg
50

326

- (2) INFORMATION FOR SEQ ID NO: 173:
  - (i) SEQUENCE CHARACTERISTICS:
    - (A) LENGTH: 376 base pairs
    - (B) TYPE: NUCLEIC ACID
    - (C) STRANDEDNESS: DOUBLE
    - (D) TOPOLOGY: LINEAR
  - (ii) MOLECULE TYPE: CDNA
  - (vi) ORIGINAL SOURCE:
    - (A) ORGANISM: Homo Sapiens
    - (F) TISSUE TYPE: Brain
  - (ix) FEATURE:
    - (A) NAME/KEY: other
    - (B) LOCATION: 74..344
    - (C) IDENTIFICATION METHOD: blastn
    - (D) OTHER INFORMATION: identity 96 region 73..343 id H95186

10 H95

- (ix) FEATURE:
  - (A) NAME/KEY: other
  - (B) LOCATION: 25..86
  - (C) IDENTIFICATION METHOD: blastn
  - (D) OTHER INFORMATION: identity 93 region 25..86

id H95186

est

- (ix) FEATURE:
  - (A) NAME/KEY: other
  - (B) LOCATION: 138..377
  - (C) IDENTIFICATION METHOD: blastn
  - (D) OTHER INFORMATION: identity 100

region 1..240

id N40665

est

- (ix) FEATURE:
  - (A) NAME/KEY: other
  - (B) LOCATION: 203..308
  - (C) IDENTIFICATION METHOD: blastn
  - (D) OTHER INFORMATION: identity 95

region 230..335

id W25197

(ix) FEATURE:

(A) NAME/KEY: sig\_peptide

WO 99/06552 PCT/IB98/01236

MO 33/00227		137		T C T/I D/G/G
7 + 5 4	LOCATION: 167 IDENTIFICATION N OTHER INFORMATIO	METHOD: Von H DN: score 7.	**	
(xi) SEQUE	ENCE DESCRIPTION	: SEQ ID NO:	173:	
AACGGCCTC GGGA	AGACGC TGCTGGTGA	A ACGGCTGCAG	GAGGTGAGCT (	CCCGGGATGG 60
GAAAGGCGAC CTGGG	GGGAGC CGCCCCGA	C ACGGCCCACG	GTGGGCACCA A	ATCTTACTGA 120
CATCGTGGCA CAGA	GAAAGA TCACCATCO	G GGAGCTTGGG	Met (	GGC CCC 175 Gly Pro .
	TAC TAT GGA AAC Tyr Tyr Gly Asn			
	CCC ACC CAG CTC Pro Thr Gln Leu -20			
	GCA GAA CAA CTT Ala Glu Gln Leu -5			
	GAC CTA CCC TGT Asp Leu Pro Cys 10			
TCA TTA ATC Ser Leu Ile				376
(2) INFORMATION	FOR SEQ ID NO:	174:		
(A) (B) (C)	NCE CHARACTERIST LENGTH: 277 bas TYPE: NUCLEIC A STRANDEDNESS: D TOPOLOGY: LINEA	e pairs CID OUBLE		
(ii) MOLE	CULE TYPE: CDNA			
(A)	INAL SOURCE: ORGANISM: Homo TISSUE TYPE: Br	•		
	NAME/KEY: other LOCATION: 592 IDENTIFICATION	278 METHOD: blas [ON: identit	y 97 28247	

est

(A) NAME/KEY: other

(B) LOCATION: 59..210

(C) IDENTIFICATION METHOD: blastn (D) OTHER INFORMATION: identity 92

region 29..180 id R64509

est

#### (ix) FEATURE:

(A) NAME/KEY: other (B) LOCATION: 196..278

(C) IDENTIFICATION METHOD: blastn

(D) OTHER INFORMATION: identity 96

region 167..249

id R64509

est

#### (ix) FEATURE:

(A) NAME/KEY: other
(B) LOCATION: 59..210

(C) IDENTIFICATION METHOD: blastn

(D) OTHER INFORMATION: identity 92

region 44..195

id H85714 est

# (ix) FEATURE:

(A) NAME/KEY: other(B) LOCATION: 196..278

(C) IDENTIFICATION METHOD: blastn

(D) OTHER INFORMATION: identity 96

region 182..264

id H85714

est

#### (ix) FEATURE:

(A) NAME/KEY: other

(B) LOCATION: 59..278

(C) IDENTIFICATION METHOD: blastn

(D) OTHER INFORMATION: identity 96

region 36..255

id H52756

est

# (ix) FEATURE:

(A) NAME/KEY: other

(B) LOCATION: 59..278

(C) IDENTIFICATION METHOD: blastn

(D) OTHER INFORMATION: identity 96

region 5..224

id H49758

est

# (ix) FEATURE:

(A) NAME/KEY: sig\_peptide

(B) LOCATION: 107..247

(C) IDENTIFICATION METHOD: Von Heijne matrix

(D) OTHER INFORMATION: score 7.9

seq LLLPRVLLTMASG/SP

(Mil JEQUENCE DESCRIPTION: SEQ ID NO: 174:

0710	$\mathtt{CGTS}$	YSGC	СТТТ	GAGA	ፐር አ	N C m C						70011	V 11 1	1010	CCGANR'	1
	CGTS												Met	Ser	Gly -45	
				-40			200	Oly	-35	val	Ala	Ser	Leu	Leu -30		
	TTT Phe		-25				LC u	-20	PIO	vai	Ala	Ser	Arg	Leu	Leu	
TTG Leu	CTA Leu	CCC Pro -10	CGA Arg	GTC Val	TTG Leu	CTG Leu	ACC Thr -5	ATG Met	GCC Ala	TCT Ser	GGA Gly	AGC Ser 1	CCT Pro	CCG Pro	ACC Thr	
CAG Gln 5	CCC Pro	TCG Ser	CCG Pro	GCC Ala	TGG Trp 10											
(2)	INFO	) SE	ION QUENC (A) I (B) I (C) S (D) I	CE CE LENGT TYPE:	HARAC TH: 3 NUC	CTER 388 L CLEIC	ISTI Dase C AC:	CS: pai:	rs							
(2)	(i	) SE i) Mc i) Os	QUENC (A) I (B) I (C) S (D) I DLECU RIGIN	CE CH LENGT TYPE: STRAN COPOL JLE T JAL S	HARACINE SHEET SHE	CTER. 388 L CLEIC NESS: LIN CDN CE: Hor	ISTIC Dase C AC: DOU NEAR NA	CS: pai; ID UBLE								
(2)	(i (i (v	i) SE i) Mo i) Os (	QUENC (A) I (B) I (C) S (D) I DLECU RIGIN (A) O F) T	CE CE LENGT TYPE: STRAN COPOL ULE T HAL S RGAN ISSU	HARACINE SHEET SHE	CTER. 388 L CLEIC NESS: LIN CDN CE: Hor	ISTIC Dase C AC: DOU NEAR NA	CS: pai; ID UBLE								
(2)	(i (i (v	i) SE  i) M( ii) OS  ( ( ( ( ( (	QUENC (A) I (B) I (C) S (D) I DLECU RIGIN	CE CH LENGT TYPE: STRAN COPOL ULE T HAL S RGAN ISSU E: AME/ OCAT DENT	HARACINE SUPPLY	CTER 388 L CLEI( VESS: LIN CDN E: Hom PE: oth 180	ISTICOASE CONTROL NO SABRAI CO	CS: pai: ID JBLE  spien  THOD  r  i	ıs	ity n 13	98	44				
(2)	(i (v (i)	i) Mc i) Mc ((((((((((((((((((((((((((((((((((((	QUENC (A) I (B) I (C) S (D) I OLECU RIGIN (A) O F) T (ATUR A) N B) L (C) I	CE CHECKE CHECKER CONTROL CONT	HARAGENE STATE STA	CTER 888 L CLEI UESS: CDN CE: Hom PE: oth 180 ATIO ORMA	ISTINDASE CONTROL ACTION NA CO	CS: pai: ID JBLE  spien  THOD  r  i	: bl dent egio d H0	ity n 13	98	4 4				

(in FRATURE:

A) NAME/KEY: sig\_peptide
DOCATION: 1137.232

(C) IDENTIFICATION METHOD: Von Heijne matrix

(D) OTHER INFORMATION: score 7.9

seq SLLLLFGGQFASS/QE

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 175:

AGCAGAGCTT CCGCTTCCGG CCCTTCAGGC TCTGTCTCTG TGGAGACTGG GCTTTGGGAG 60

GKAGAAAGAG GGACCTAGCG CGGGCCGCGC AGGCGCACGG TGGGCAGCTG CA ATG GCG 118

Met Ala
-40

CTG TCG TGT ACC CTT AAC AGG TAT CTG CTC CTC ATG GCG CAG GAG CAT
Leu Ser Cys Thr Leu Asn Arg Tyr Leu Leu Leu Met Ala Gln Glu His
-35
-30
-25

CTG GAG TTC CGC CTG CCG GAA ATA RRG TCT TTG CTT TTG CTT TTT GGA
Leu Glu Phe Arg Leu Pro Glu Ile Xaa Ser Leu Leu Leu Leu Phe Gly
-20
-15
-10

GGT CAG TTT GCC AGC AGT CAA GAA ACT TAT GGA AAG TCA CCA TTT TGG
Gly Gln Phe Ala Ser Ser Gln Glu Thr Tyr Gly Lys Ser Pro Phe Trp

ATT CTT AGC ATT CCC TCT GAA GAT ATT GCA AGA AAT TTG ATG AAA CGG

Ile Leu Ser Ile Pro Ser Glu Asp Ile Ala Arg Asn Leu Met Lys Arg

15 20 25

ACA GTG TGT GCC AAG TCT ATA TTT GAA CTA TGG GGT CAT GGA CAA TCT

Thr Val Cys Ala Lys Ser Ile Phe Glu Leu Trp Gly His Gly Gln Ser

30

35

40

CCT GAG GAG CTG TAC AGT TCT CTT AAA AAC
Pro Glu Glu Leu Tyr Ser Ser Leu Lys Asn
45 50

- (2) INFORMATION FOR SEQ ID NO: 176:
  - (i) SEQUENCE CHARACTERISTICS:
    - (A) LENGTH: 311 base pairs
    - (3) TYPE: NUCLEIC ACID
    - (C) STRANDEDNESS: DOUBLE
    - (D) TOPOLOGY: LINEAR
  - (ii) MOLECULE TYPE: CDNA
  - (vi) ORIGINAL SOURCE:
    - (A) ORGANISM: Homo Sapiens
    - (F) TISSUE TYPE: Brain
  - (ix) FEATURE:
    - (A) NAME/KEY: other
    - (E) LOCATION: 112..309
    - (C) IDENTIFICATION METHOD: blastn
    - (D) OTHER INFORMATION: identity 97 region 69..266 id AA149265

CINE FEATURE: (A) NAME/KEY: other (B) LOCATION: 41..86 (C) IDENTIFICATION METHOD: blastn (D) OTHER INFORMATION: identity 97 region 1..46 id AA149265 est (ix) FEATURE: (A) NAME/KEY: other (B) LOCATION: 110..309 (C) IDENTIFICATION METHOD: blastn (D) OTHER INFORMATION: identity 97 region 53..252 id W39570 est (ix) FEATURE: (A) NAME/KEY: other (B) LOCATION: 56..86 (C) IDENTIFICATION METHOD: blastn (D) OTHER INFORMATION: identity 96 region 2..32 id W39570 est (ix) FEATURE: (A) NAME/KEY: other (B) LOCATION: 110..309 (C) IDENTIFICATION METHOD: blastn (D) OTHER INFORMATION: identity 97 region 55..254 id N41332 est (ix) FEATURE: (A) NAME/KEY: other (B) LOCATION: 53..86 (C) IDENTIFICATION METHOD: blastn (D) OTHER INFORMATION: identity 97 region 1..34 id N41332 est (111) FEATURE: (A) NAME/KEY: sig\_peptide (B) LOCATION: 39..197 (C) IDENTIFICATION METHOD: Von Heijne matrix (D) OTHER INFORMATION: score 7.1 seq IAVGLGVAALAFA/GR (W1) SEQUENCE DESCRIPTION: SEQ ID NO: 176:

AACCU COUNT GOGGOTTGAG TOTOCGGGCC GCCTTGCC ATG GCT GCC CGT GGT GTC

56

Met Ala Ala Arg Gly Val

Ile Ala Pro Val Gly Glu Ser Leu Arg Tyr Ala Glu Tyr Leu Gln Pro
-45 -40 -35

TCG GCC AAA CGG CCA GAC GCC GAC GTC GAC CAG CAG AGA CTG GTA AGA

Ser Ala Lys Arg Pro Asp Ala Asp Val Asp Gln Gln Arg Leu Val Arg

-30

-25

-20

AGT TTG ATA GCT GTA GGA CTG GGT GTT GCA GCT CTT GCA TTT GCA GGT

Ser Leu Ile Ala Val Gly Leu Gly Val Ala Ala Leu Ala Phe Ala Gly

-15

-5

1

CGC TAC GCA TTT CGG ATC TGG AAA CCT CTA GAA CAA GTT ATC ACA GAA
Arg Tyr Ala Phe Arg Ile Trp Lys Pro Leu Glu Gln Val Ile Thr Glu
5 10 15

ACT GCA AAG AAG ATT TCA ACT CCT AGC TTT TCA TCC TAC TAT AAA GGA
Thr Ala Lys Lys Ile Ser Thr Pro Ser Phe Ser Ser Tyr Tyr Lys Gly
20 25 30

GGA TTT GAA CGG AGG Gly Phe Glu Arg Arg 35

311

#### (2) INFORMATION FOR SEO ID NO: 177:

- (i) SEQUENCE CHARACTERISTICS:
  - (A) LENGTH: 384 base pairs
  - (B) TYPE: NUCLEIC ACID
  - (C) STRANDEDNESS: DOUBLE
  - (D) TOPOLOGY: LINEAR
- (ii) MOLECULE TYPE: CDNA
- (vi) ORIGINAL SOURCE:
  - (A) ORGANISM: Homo Sapiens
  - (F) TISSUE TYPE: Brain
- (ix) FEATURE:
  - (A) NAME/KEY: other
  - (B) LOCATION: 43..87
  - (C) IDENTIFICATION METHOD: blastn
  - (D) OTHER INFORMATION: identity 100 region 8..52 id W32101
- (ix) FEATURE:
  - (A) NAME/KEY: other
  - (B) LOCATION: 89..129
  - (C) IDENTIFICATION METHOD: blastn
  - (D) OTHER INFORMATION: identity 100 region 53..93 id W32101
- (1:) FEATURE:
  - (A) NAME/KEY: sig\_peptide
  - (B) LOCATION: 292..375
  - (C) IDENTIFICATION METHOD: Von Heijne matrix

(D) OTHER INFORMATION: score 6.6

seq VLGXLFLGGLCRG/WD

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 177:

AAGAGCCGCG TTYAGTCTAT CGCTGCGGTT GCGAGCGCTG TAGGGAGCCT GTGCTGTGCC 60
GCGCAGTTAG GCAGCAGCAG CCGCGGAGCA GTAGCCGCCG TGGGAGGGAG CCATGAAGCA 120
TTACGAGGTA AGAAGCGAGA AACAGGGGCC GTGTGGCCAC TGCTGACCCA TTCTTTTTCC 180
TTCTTTGCGG GACCACGGGA CCCCACTTTC TGGTCCTGTG CCCCGAAGGA AGAKCCAGAC 240
GGCGCAGGCG CAGTGGGCAA GCGTTGCGCC CCGGGCCACT CGTAAATTCC A ATG CGC 297
Met Arg

ATG TGC GCA GGA AGT ATT TAT AAA TCT GCA ACC CAG GCT GTT TTG GGG 345
Met Cys Ala Gly Ser Ile Tyr Lys Ser Ala Thr Gln Ala Val Leu Gly -25 -20 -15

GWA CTT TTT CTT GGG GGT CTC TGC AGG GGC TGG GAC GCT 384

CTA CTA CTT CTT GGG GGT CTC TGC AGG GGC TGG GAC GCT 384

CTA CTA CTT CTT CTT GGG GGT CTC TGC AGG GGC TGG GAC GCT 384

CTA CTT CTT CTT GGG GGT CTC TGC AGG GGC TGG GAC GCT 384

CTA CTT CTT CTT GGG GGT CTC TGC AGG GGC TGG GAC GCT 384

CTA CTT CTT CTT GGG GGT CTC TGC AGG GGC TGG GAC GCT 384

# (2) INFORMATION FOR SEQ ID NO: 178:

- (i) SEQUENCE CHARACTERISTICS:
  - (A) LENGTH: 425 base pairs
  - (B) TYPE: NUCLEIC ACID
  - (C) STRANDEDNESS: DOUBLE
  - (D) TOPOLOGY: LINEAR
- (ii) MOLECULE TYPE: CDNA
- (vi) ORIGINAL SOURCE:
  - (A) ORGANISM: Homo Sapiens
  - (F) TISSUE TYPE: Brain
- (ix) FEATURE:
  - (A) NAME/KEY: other
  - (B) LOCATION: 73..317
  - (C) IDENTIFICATION METHOD: blastn
  - (D) OTHER INFORMATION: identity 97 region 1..245

id HUM506F10B

est

- (ix) FEATURE:
  - (A) NAME/KEY: other
  - (3) LOCATION: 314..376
  - (C) IDENTIFICATION METHOD: blastn
  - (D) OTHER INFORMATION: identity 98 region 243..305

id HUM506F10B

est

- (ix) FEATURE:
  - (A) NAME/KEY: other

- (B) LOCATION: 63..193
- (C) IDENTIFICATION METHOD: blastn
- (D) OTHER INFORMATION: identity 99 region 1..131

id AA056148 est

#### (ix) FEATURE:

- (A) NAME/KEY: other
- (B) LOCATION: 314..401
- (C) IDENTIFICATION METHOD: blastn
- (D) OTHER INFORMATION: identity 95

region 254..341

id AA056148

est

#### (ix) FEATURE:

- (A) NAME/KEY: other
- (B) LOCATION: 277..317
- (C) IDENTIFICATION METHOD: blastn
- (D) OTHER INFORMATION: identity 97

region 216..256

id AA056148

est

#### (ix) FEATURE:

- (A) NAME/KEY: other
- (3) LOCATION: 397..426
- (C) IDENTIFICATION METHOD: blastn
- (D) OTHER INFORMATION: identity 96

region 338..367

id AA056148

est

# (ix) FEATURE:

- (A) NAME/KEY: other
- (B) LOCATION: 88..189
- (C) IDENTIFICATION METHOD: blastn
- (D) OTHER INFORMATION: identity 98

region 1..102 id HSC1FF051

est

## (ix) FEATURE:

- (A) NAME/KEY: other
- (B) LOCATION: 314..401
- (C) IDENTIFICATION METHOD: blastn

(D) OTHER INFORMATION: identity 96

region 230..317

id HSC1FF051

est

### (ix) FEATURE:

- (A) NAME/KEY: other
- (3) LOCATION: 187..271
- (C) IDENTIFICATION METHOD: blastn
- (D) OTHER INFORMATION: identity 95

region 101..185

id HSC1FF051

est

145 (ix) FEATURE: (A) NAME/KEY: other (B) LOCATION: 269..317 (C) IDENTIFICATION METHOD: blastn (D) OTHER INFORMATION: identity 93 region 184..232 id HSC1FF051 est (ix) FEATURE: (A) NAME/KEY: other (B) LOCATION: 397..426 (C) IDENTIFICATION METHOD: blastn (D) OTHER INFORMATION: identity 96 region 314..343 id HSC1FF051 est (ix) FEATURE: (A) NAME/KEY: other (B) LOCATION: 87..200 (C) IDENTIFICATION METHOD: blastn (D) OTHER INFORMATION: identity 92 region 1..114 id HSC16E081 est (ix) FEATURE: (A) NAME/KEY: other (B) LOCATION: 314..401 (C) IDENTIFICATION METHOD: blastn (D) OTHER INFORMATION: identity 96 region 231..318 id HSC16E081 (ix) FEATURE: (A) NAME/KEY: other (B) LOCATION: 199..275 (C) IDENTIFICATION METHOD: blastn (D) OTHER INFORMATION: identity 94 region 114..190 id HSC16E081 est (ix) FEATURE: (A) NAME/KEY: other (B) LOCATION: 269..317 (C) IDENTIFICATION METHOD: blastn (D) OTHER INFORMATION: identity 91 region 185..233 id HSC16E081 (ix) FEATURE: (A) NAME/KEY: other (B) LOCATION: 397..426 (C) IDENTIFICATION METHOD: blastn (D) OTHER INFORMATION: identity 96 region 315..344

1d HSC16E081

est

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- 4	Ίi	.,	٦.	Ľ	С	л	T	7	2	Ε	٠

- (A) NAME/KEY: other
- (B) LOCATION: 85..186
- (C) IDENTIFICATION METHOD: blastn
  (D) OTHER INFORMATION: identity 99

region 24..125 id AA157365

est

#### (ix) FEATURE:

- (A) NAME/KEY: other
- (B) LOCATION: 183..263
- (C) IDENTIFICATION METHOD: blastn
- (D) OTHER INFORMATION: identity 90

region 123..203

id AA157365

est

#### (ix) FEATURE:

- (A) NAME/KEY: other
- (B) LOCATION: 337..401
- (C) IDENTIFICATION METHOD: blastn
- (D) OTHER INFORMATION: identity 95

region 278..342

id AA157365

est

#### (ix) FEATURE:

- (A) NAME/KEY: other
- (B) LOCATION: 273..326
- (C) IDENTIFICATION METHOD: blastn
  - (D) OTHER INFORMATION: identity 90

region 213..266

id AA157365

est

# (ix) FEATURE:

- (A) NAME/KEY: sig\_peptide
- (B) LOCATION: 186..419
- (C) IDENTIFICATION METHOD: Von Heijne matrix
- (D) OTHER INFORMATION: score 6.3

seq TLIMLLSWQLSVS/SV

#### (xi) SEQUENCE DESCRIPTION: SEO ID NO: 178:

AATGCGCGCT CGCGNTCCCG CCCTCTAGCT GCGCTCGGCT GAGTCAGTCA GTCTGTCGGA 60

STCTGTCCTC GGAGCAGGCG GAGTAAAGGG ACTTGAGCGA GCCAGTTGCC GGATTATTCT 120

ATTTCCCCTC CCTCTCCCC GCCCCGTATC TCTTTTCACC CTTCTCCCAC CCTCGCTCGC 180

TASC ATG GCG GAG CGT CGG CGG CCA CTC AGT CCC ATT CCA TCT NNT CGT 230

Met Ala Glu Arg Arg Pro Leu Ser Pro Ile Pro Ser Xaa Arg

-75 -70 -65

Arg Pro Ser Glu Pro Ser Arg Pro Arg Pro Ala Ala Ala Gly Xaa Arg
-50 -50

ADD CTG CCC CAN CCT GGG GAC GAA GAG CTG CAG CTC CAN TGT GCG GTG 326 Ser Leu Pro Ard Pro Gly Asp Glu Glu Leu Gln Leu Eto Cys Ala Val -40 -45 CAC GAT CTG ATT TTC TGG AGA GAT GTG AAG AAG ACT GGG TTT GTC TTT 374 His Asp Leu Ile Phe Trp Arg Asp Val Lys Lys Thr Gly Phe Val Phe -25 GGC ACC ACG CTG ATC ATG CTG CTT TCC TGG CAG CTT TCA GTG TCA TCA 422 Gly Thr Thr Leu Ile Met Leu Leu Ser Trp Gln Leu Ser Val Ser Ser -10 GTG 425 Val

# (2) INFORMATION FOR SEQ ID NO: 179:

#### (i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 403 base pairs
- (B) TYPE: NUCLEIC ACID
- (C) STRANDEDNESS: DOUBLE
- (D) TOPOLOGY: LINEAR
- (ii) MOLECULE TYPE: CDNA

#### (vi) ORIGINAL SOURCE:

- (A) ORGANISM: Homo Sapiens
- (F) TISSUE TYPE: Brain

#### (ix) FEATURE:

- (A) NAME/KEY: other
- (B) LOCATION: 105..351
- (C) IDENTIFICATION METHOD: blastn
- (D) OTHER INFORMATION: identity 98

region 49..295 id R47336

est

#### (ix) FEATURE:

- (A) NAME/KEY: other
- (B) LOCATION: 58..107
- (C) IDENTIFICATION METHOD: blastn
- (D) OTHER INFORMATION: identity 98

region 1..50 id R47336

est

#### (ix) FEATURE:

- (A) NAME/KEY: other
- (B) LOCATION: 352..381
- (C) IDENTIFICATION METHOD: blastn
- (D) OTHER INFORMATION: identity 100 region 295..324

id R47336 est

# (ix) FEATURE:

(A) NAME/KEY: sig\_peptide

(B) LOCATION: 5..331 (C) IDENTIFICATION METHOD: Von Heijne matrix

(D) OTHER INFORMATION: score 6

seq LQLLLGMTASAVA/AL

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 179:

AAAG			. Leu			Val		GAG Glu -95	49
CGG Arg									97
	TAC Tyr								145
	TGC Cys -60								193
	TGG Trp						 	 	241
	GTA Val								289
	CAG Gln								337
	ATG Met 5							TGG Trp	385
	TTC Phe								403

# (2) INFORMATION FOR SEQ ID NO: 180:

20

- (i) SEQUENCE CHARACTERISTICS:
  - (A) LENGTH: 367 base pairs
  - (B) TYPE: NUCLEIC ACID
  - (C) STRANDEDNESS: DOUBLE
  - (D) TOPOLOGY: LINEAR
- (ii) MOLECULE TYPE: CDNA
- (vi) ORIGINAL SOURCE:
  - (A) ORGANISM: Homo Sapiens
  - (F) TISSUE TYPE: Brain
- (ix) FEATURE:

(A) NAME/KEY: other

(B) LOCATION: 110...260

(C) IDENTIFICATION METHOD: blastn

(D) OTHER INFORMATION: identity 92

region 121..269 id W31320

est

#### (ix) FEATURE:

(A) NAME/KEY: other

- (B) LOCATION: 47..118
- (C) IDENTIFICATION METHOD: blastn

(D) OTHER INFORMATION: identity 100

region 57..128 id W31320

est

# (ix) FEATURE:

(A) NAME/KEY: other

- (B) LOCATION: 273..333
- (C) IDENTIFICATION METHOD: blastn

(D) OTHER INFORMATION: identity 93

region 282..342

id W31320 est

#### (ix) FEATURE:

(A) NAME/KEY: other

- (B) LOCATION: 107..260
- (C) IDENTIFICATION METHOD: blastn

(D) OTHER INFORMATION: identity 98

region 2..155

id T27259

est

# (ix) FEATURE:

(A) NAME/KEY: other

(B) LOCATION: 273..369

(C) IDENTIFICATION METHOD: blastn

(D) OTHER INFORMATION: identity 100

region 168..264

id T27259

est

# (ix) FEATURE:

(A) NAME/KEY: other

(B) LOCATION: 145..260

(C) IDENTIFICATION METHOD: blastn

(D) OTHER INFORMATION: identity 90

region 108..223

id AA157646

est

#### (ix) FEATURE:

(A) NAME/KEY: other

(B) LOCATION: 59..118

(C) IDENTIFICATION METHOD: blastn

(D) OTHER INFORMATION: identity 90 region 25..84

id AA157646

est

65

367

Glu

	(i		(B) (C)	NAME LOCA IDEN	TION TIFI	: ot : 27 CATI FORM	33 ON M	ETHO N:	iden	tity on 2	94 45	279				
	(i	x) F	(B) (C)	NAME LOCA IDEN	TION TIFI	: si : 50 CATI FORM	15 ON M	1 ETHO	D: V scor	e 5.	eijn 9 ALAL					
	( x	i) S	EQUE	NCE	DESC	RIPT	ION:	SEC	DI	NO:	180:					
AAT <i>I</i>	таст	TC I	TTGI	CAAG	SA GA	AGCA	GAGG	TG1	GGAC	GCT	GTGT	'ATGA			T TTC	58
	CAG Gln -30															106
	GCC Ala															154
	TTT Phe															202
	GAC Asp															250
	CTA Leu 35															298
GGC	TGT	TTC	CTC	TGT	CGA	GAG	GAA	GCT	GCG	GAT	CTG	TCC	TCC	CTG	AAA	346

# (2) INFORMATION FOR SEQ ID NO: 181:

70

AGC ATG TTG GAC CAG CTG GGC

Ser Met Leu Asp Gln Leu Gly

- (i) SEQUENCE CHARACTERISTICS:
  - (A) LENGTH: 257 base pairs

Gly Cys Phe Leu Cys Arg Glu Glu Ala Ala Asp Leu Ser Ser Leu Lys

- (B) TYPE: NUCLEIC ACID
- (C) STRANDEDNESS: DOUBLE
- (D) TOPOLOGY: LINEAR

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151
 (13) MOLECULE TYPE: CDNA
 (vi) ORIGINAL SOURCE:
      (A) ORGANISM: Homo Sapiens
       (F) TISSUE TYPE: Brain
 (ix) FEATURE:
       (A) NAME/KEY: other
       (B) LOCATION: 138..257
       (C) IDENTIFICATION METHOD: blastn
      (D) OTHER INFORMATION: identity 98
                               region 93..202
                               id W31692
                               est
(ix) FEATURE:
      (A) NAME/KEY: other
      (B) LOCATION: 55..131
      (C) IDENTIFICATION METHOD: blastn
      (D) OTHER INFORMATION: identity 100
                              region 1..77
                              id W31692
                               est
(ix) FEATURE:
      (A) NAME/KEY: other
      (B) LOCATION: 136..257
      (C) IDENTIFICATION METHOD: blastn
      (D) OTHER INFORMATION: identity 98
                              region 78..199
                              id H50194
                              est
(ix) FEATURE:
      (A) NAME/KEY: other
      (B) LOCATION: 57..131
      (C) IDENTIFICATION METHOD: blastn
      (D) OTHER INFORMATION: identity 100
                              region 1..75
                              id H50194
                              est
(ix) FEATURE:
     (A) NAME/KEY: other
      (B) LOCATION: 57..257
      (C) IDENTIFICATION METHOD: blastn
     (D) OTHER INFORMATION: identity 97
                              region 1..201
                              id H46855
                              est
(ix) FEATURE:
     (A) NAME/KEY: other
     (B) LOCATION: 138..257
     (C) IDENTIFICATION METHOD: blastn
     (D) OTHER INFORMATION: identity 98
                              region 81..200
                              id H49687
```

est

(ix) FEATURE:

		(B	) L(	OCAT DENT	ION: IFIC		.132 N ME	THOD I: i r i	o: bl dent egio d H4	ity n 1.	100 .76					
	(ix	(B	() N () L () I	AME/ OCAT DENT	ION:	oth 138 CATIC	25 N ME	THOE I: i	): bl ident regio id TS	ity on 80	98 )19	9				
	(ix	(E	A) N B) L C) I	ame/ OCAI DENI	ION:		.124 N M	ETHOI N:	D: blident regio id T! est	city on 2	100 68					
		(E	A) N B) L C) I D) C	OCAT OCAT DENT	rion rifi R in	FORM	20 ON M	O ETHO N:	D: Vescore	e 4. MLIM	9 LGIF					
ATCT	'CTGC	àc cc	CTG	CGAG	G GC	ATCC	TGGG	стт	TCTC	CCA	CCGC	TTTC	CG A	.GCCC	GCTTG	60
		CG AT						ATG		TCG	CTC	CTG	TGC	TGT	GGG	113
		CTG G Leu A	la i													161
		ATA A Ile M														209
		GAC C Asp V														257
(2)			QUEN (A)	ICE (	CHARI		RIST	ICS: e pa	irs							

(ii) MOLECULE TYPE: CDNA

(vi) ORIGINAL SOURCE:

- (A) ORGANISM: Homo Sapiens
- (F) TISSUE TYPE: Brain
- (ix) FEATURE:
  - (A) NAME/KEY: other
  - (B) LOCATION: 365..401
  - (C) IDENTIFICATION METHOD: blastn
  - (D) OTHER INFORMATION: identity 100 region 1..37 id R50224 est

- (ix) FEATURE:
  - (A) NAME/KEY: sig\_peptide
  - (B) LOCATION: 305..364
  - (C) IDENTIFICATION METHOD: Von Heijne matrix
  - (D) OTHER INFORMATION: score 4.9 seq XSLFLHAVSSSFT/QL
- (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 182:

ATGACCACGG GTTTAACCTT CTTATCCCAG AGACACCCAA TTCTAGAGCT TTATGGAGCC 60 GTACTTCCCC CTGAATCCTA GCTCTAGGAC ATAGATCATG ACTCTCAGCC CTTTTACCCA 120 GGATGGAGCT GGGGCCTGTA TAGCCATATT ATTGTTCTAA GTAAGTTCTA GCCCCACCCT 180 CCCGCCTTCT TGAGTGATAC CTATTACGGA TGAGTTCTGG AAAAGACCCA GCTATGATTC ATAAAAACAC TTCTGGATGA ATCAAGAACC ATTTCTTGTT TKTCCTAGAT AATTCTCTAA 300 AAAT ATG ATT CTT CCA TAT AGA ATG CKA AGC TTA TTT TTA CAT GCA GTT 349 Met Ile Leu Pro Tyr Arg Met Xaa Ser Leu Phe Leu His Ala Val TCT AGC TCC TTC ACC CAG CTG AGG TCG TGC CAG GGA GAC AGA GTC TGG Ser Ser Ser Phe Thr Gln Leu Arg Ser Cys Gln Gly Asp Arg Val Trp 397 1 AGA

400

(2) INFORMATION FOR SEQ ID NO: 183:

Arg

- (i) SEQUENCE CHARACTERISTICS:
  - (A) LENGTH: 256 base pairs
  - (B) TYPE: NUCLEIC ACID
  - (C) STRANDEDNESS: DOUBLE
  - (D) TOPOLOGY: LINEAR
- (ii) MOLECULE TYPE: CDNA

	· , , , , , , , , , , , , , , , , , , ,						154					• • •	
	(vi)		NAL SOU ORGANIS TISSUE	SM: Ho			ns						
	(ix)	(B) :	RE: NAME/KI LOCATIO IDENTII OTHER	ON: 86 FICATI	18 ON M	etho N:	D: b iden regi id A est	tity on 5	93 10	5			
	(ix)	FEATU											
			NAME/KI LOCATIO				e						
			IDENTI				D: V	on H	eijn	e ma	trix		
		(D)	OTHER	INFORM	1ATIO		scor seq			ĆD N LJ	n /nu		
							seq	PIIA	KALA	GRAW	A/AV		
	(xi)	SEQUE	NCE DE	SCRIP	: NOI	SEC	ID	NO:	183:				
				ma 3.5								 	
AGAA	G I GCG	r sycgo	CGGGA					Val				Ser	52
		TC GAG eu Glu -50											100
	Ser A	GG GTC rg Val 35											148
		GA CAT rg His			Thr								196
		CC TGG la Trp											244
		CC TGG ro Trp 15											256
(2)	INFOR	MATION	FOR S	EQ ID	NO:	184:							

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 352 base pairs

(B) TYPE: NUCLEIC ACID

(C) STRANDEDNESS: DOUBLE

(D) TOPOLOGY: LINEAR

(ii) MOLECULE TYPE: CDNA

(vi) ORIGINAL SOURCE:

(A) ORGANISM: Homo Sapiens

(F) TISSUE TYPE: Brain

```
(ix) FEATURE:
```

- (A) NAME/KEY: other
- (B) LOCATION: 183..348
- (C) IDENTIFICATION METHOD: blastn
- (D) OTHER INFORMATION: identity 98 region 78..243

id W52941

# (ix) FEATURE:

- (A) NAME/KEY: other
- (B) LOCATION: 286..348
- (C) IDENTIFICATION METHOD: blastn
- (D) OTHER INFORMATION: identity 96 region 1..63 id H55390

est

#### (ix) FEATURE:

- (A) NAME/KEY: sig\_peptide
- (B) LOCATION: 77..199
- (C) IDENTIFICATION METHOD: Von Heijne matrix
- (D) OTHER INFORMATION: score 4.7

seq LFSCFCFLSHKFG/KK

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 184:

# AAAAAATATC TCCCGGCGTG CGCTGCTTGT GTTATGTTCG GGTTTTAAGT CGTGTCAGCG 60

- TTTACATTTT CTTAAT ATG AAA AAT GCC TGC ATT GTT CTG CCG CCA ACT CCC 112

  Met Lys Asn Ala Cys Ile Val Leu Pro Pro Thr Pro

  -40 -35 -30
- CCT CCC TCC CTG CAA CCC TCG GCC TCT CTG CTG GCG CCT AAT CGT TTT

  Pro Pro Ser Leu Gln Pro Ser Ala Ser Leu Leu Ala Pro Asn Arg Phe

  -25

  -15
- TTA TTC TCT TGC TTC TGC TTT CTT AGT CAC AAG TTT GGG AAG AAA GTC
  Leu Phe Ser Cys Phe Cys Phe Leu Ser His Lys Phe Gly Lys Lys Val
- ATC TAT TTC AAC TAC CTG AGT GAG CTC CAC GAA CAC CTT AAA TAC GAC

  11e Tyr Phe Asn Tyr Leu Ser Glu Leu His Glu His Leu Lys Tyr Asp

  15
- CAG CTG GTC ATC CCT CCC GAA GTT TTG CGG TAC GAT GAG AAG CTC CAG
  Gln Leu Val Ile Pro Pro Glu Val Leu Arg Tyr Asp Glu Lys Leu Gln
  20 25 30
- AGC CTG CAC GAG GGC CGG ACG CCG MCT CCC ACC AAG ACA CCA CCA GGG Ser Leu His Glu Gly Arg Thr Pro Xaa Pro Thr Lys Thr Pro Pro Gly 45

# (2) INFORMATION FOR SEQ ID NO: 185:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 274 base pairs
- (B) TYPE: NUCLEIC ACID
- (C) STRANDEDNESS: DOUBLE
- (D) TOPOLOGY: LINEAR
- (ii) MOLECULE TYPE: CDNA
- (vi) ORIGINAL SOURCE:
  - (A) ORGANISM: Homo Sapiens
  - (F) TISSUE TYPE: Brain
- (ix) FEATURE:
  - (A) NAME/KEY: other
  - (B) LOCATION: 99..260
  - (C) IDENTIFICATION METHOD: blastn
  - (D) OTHER INFORMATION: identity 96

region 126..287

id T53519

est

- (ix) FEATURE:
  - (A) NAME/KEY: other
  - (B) LOCATION: 40..108
  - (C) IDENTIFICATION METHOD: blastn
  - (D) OTHER INFORMATION: identity 91

region 1..69

id T53519

est

- (ix) FEATURE:
  - (A) NAME/KEY: other
  - (B) LOCATION: 113..269
  - (C) IDENTIFICATION METHOD: blastn
  - (D) OTHER INFORMATION: identity 96

region 131..287

id W87344

est

- (ix) FEATURE:
  - (A) NAME/KEY: other
  - (B) LOCATION: 147..269
  - (C) IDENTIFICATION METHOD: blastn
  - (D) OTHER INFORMATION: identity 96

region 138..260

id N56542

est

- (ix) FEATURE:
  - (A) NAME/KEY: other
  - (B) LOCATION: 113..149
  - (C) IDENTIFICATION METHOD: blastn
  - (D) OTHER INFORMATION: identity 91

region 105..141

id N56542

est

- (ix) FEATURE:
  - (A) NAME/KEY: other
  - (B) LOCATION: 75..105
  - (C) IDENTIFICATION METHOD: blastn
  - (D) OTHER INFORMATION: identity 96

WO 99/06552	PCT/IB98/01236
WU 99/06552	PC 1/1B98/01230

157 region 1..31 id N56542 (ix) FEATURE: (A) NAME/KEY: other (B) LOCATION: 113..218 (C) IDENTIFICATION METHOD: blastn (D) OTHER INFORMATION: identity 96 region 117..222 id AA053475 est (ix) FEATURE: (A) NAME/KEY: other (B) LOCATION: 218..269 (C) IDENTIFICATION METHOD: blastn (D) OTHER INFORMATION: identity 94 region 223..274 id AA053475 est (ix) FEATURE: (A) NAME/KEY: other (B) LOCATION: 113..269 (C) IDENTIFICATION METHOD: blastn (D) OTHER INFORMATION: identity 95 region 90..246 id W05444 est (ix) FEATURE: (A) NAME/KEY: sig\_peptide (B) LOCATION: 110..193 (C) IDENTIFICATION METHOD: Von Heijne matrix (D) OTHER INFORMATION: score 4.6 seg PLQWSLLVAVVAG/SV (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 185: ACTTCCGCCT GCGCCTGCGC AGCVCAGCTC CSHGAGCCCT GCCAACCATG GTGAACTTGG GTCTGTCCCG GGTGGACGAC GCCGTGGCTG CCAAGCACCC GGCACCGGC ATG GCC TTT 118 Met Ala Phe GGC TTG CAG ATG TTC ATT CAG AGG AAG TTT CCA TAC CCT TTG CAG TGG Gly Leu Gln Met Phe Ile Gln Arg Lys Phe Pro Tyr Pro Leu Gln Trp -25 -20 -15 AGC CTC CTA GTG GCC GTG GTT GCA GGC TCT GTG GTC AGC TAC GGG GTG 214 Ser Leu Leu Val Ala Val Val Ala Gly Ser Val Val Ser Tyr Gly Val ACG AGA GTR RAG TOG GAG AAA TGC AAC AAC CTC TGG CTC TTC CTG GAG Thr Arg Val Xaa Ser Glu Lys Cys Asn Asn Leu Trp Leu Phe Leu Glu

15

274

ACC GGA CTT GGG Inr Gly Leu Gly 25

10

(2) INFORMATION FOR SEQ ID NO: 186:								
(i) SEQUENCE CHARACTERISTICS:  (A) LENGTH: 316 base pairs  (B) TYPE: NUCLEIC ACID  (C) STRANDEDNESS: DOUBLE  (D) TOPOLOGY: LINEAR								
(ii) MOLECULE TYPE: CDNA								
<pre>(vi) ORIGINAL SOURCE:    (A) ORGANISM: Homo Sapiens    (F) TISSUE TYPE: Brain</pre>								
(ix) FEATURE:  (A) NAME/KEY: other  (B) LOCATION: 45315  (C) IDENTIFICATION METHOD: blastn  (D) OTHER INFORMATION: identity 98  region 1271  id HSC1ZD051  est								
<pre>(ix) FEATURE:     (A) NAME/KEY: sig_peptide     (B) LOCATION: 110268     (C) IDENTIFICATION METHOD: Von Heijne matrix     (D) OTHER INFORMATION: score 4.5</pre>								
ATATGAGACT CTGGCCTCCC TGCAGATCTT CTAAGAACCA CACTAATGCA AGCGTGACAG	60							
AGAAACCTCT TTCGAATGAC CTACTACAAC TCTGGCATTG GTTAGTTCC ATG TAT TGT Met Tyr Cys	118							
AAG ATT CTG GTG CTA ATG CTC CAT ACA GAA TTG ATC AGG ACT GAT TAC Lys Ile Leu Val Leu Met Leu His Thr Glu Leu Ile Arg Thr Asp Tyr -50 -45 -40 -35	166							
TCT TCT GTG GAC CAA TTG CTA TTG AAC TAC CCA GCT GAA GAG GGT TTG Ser Ser Val Asp Gln Leu Leu Asn Tyr Pro Ala Glu Glu Gly Leu -30 -25 -20	214							
GGG AGA GAA CGT TCA TTA TTA TGG ACT CCA CTT TTG TCS CCT GGT AGT Gly Arg Glu Arg Ser Leu Leu Trp Thr Pro Leu Leu Ser Pro Gly Ser -15 -10 -5	262							
TTA AGG GTG ATA CTA GAA TCC AGA GAA GTT CCT GTC TCC TTG TGG CCC Leu Arg Val Ile Leu Glu Ser Arg Glu Val Pro Val Ser Leu Trp Pro  1 5 10	310							
CAA ACG Gln Thr 15	316							

region 189..267 id W81202 est

(2) INFORMATION FOR SEQ ID NO: 187: (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 423 base pairs (B) TYPE: NUCLEIC ACID (C) STRANDEDNESS: DOUBLE (D) TOPOLOGY: LINEAR (ii) MOLECULE TYPE: CDNA (vi) ORIGINAL SOURCE: (A) ORGANISM: Homo Sapiens (F) TISSUE TYPE: Brain (ix) FEATURE: (A) NAME/KEY: other (B) LOCATION: 50..246 (C) IDENTIFICATION METHOD: blastn (D) OTHER INFORMATION: identity 96 region 1..197 id AA043070 est (ix) FEATURE: (A) NAME/KEY: other (B) LOCATION: 241..373 (C) IDENTIFICATION METHOD: blastn (D) OTHER INFORMATION: identity 97 region 191..323 id AA043070 est (ix) FEATURE: (A) NAME/KEY: other (B) LOCATION: 371..408 (C) IDENTIFICATION METHOD: blastn (D) OTHER INFORMATION: identity 100 region 322..359 id AA043070 (ix) FEATURE: (A) NAME/KEY: other (B) LOCATION: 186..357 (C) IDENTIFICATION METHOD: blastn (D) OTHER INFORMATION: identity 95 region 29..200 id W81202 est (ix) FEATURE: (A) NAME/KEY: other (B) LOCATION: 345..423 (C) IDENTIFICATION METHOD: blastn (D) OTHER INFORMATION: identity 100

(ix) FEATURE:

			(B) (C)	NAME LOCA' IDEN' OTHE	TION TIFI	: 64 CATI	17 ON M	ETHO	D: b iden regional id Wi est	tity on 8:	100 51	98				
	(i		(A) (B) (C)	RE: NAME LOCA IDEN OTHE	TION TIFI	: 17 CATI	82: ON M	ETHO N:	D: b iden regi id W est	tity on 1	90 98	247				
			(A) (B) (C) (D)	RE: NAME LOCA IDEN OTHE	TION TIFI R IN	: 16 CATI FORM	62 ON M ATIO	43 ETHO N:	D: V scor seq	e 4. ENSL	5 IILL	QGLQ				
AACT	CTGC	GC C	CGGA	GGAC	A GA	GCGG	CCCG	GTC	GCCG	GCA	TGGT	TTCT	cc c	STCCI	GCTGC	60
AGCC	GGCG	GG A	.GGCA	AGCC#	G TC	CAGG	CGCC	CGC	TAGO	TTC	GGCG	GCGA	cc c	CAGAC	GGGGA	120
AAGC	GGAA	.GG A	ATGI	CGCG	ST GO	AAGO	AGGC	: AGC	CTGGI	GTG	GAAC		t Al		G AGC	177
				GAG Glu												225
				CAG Gln												273
AGC Ser	GTG Val	GCC Ala	CAC His	GGA Gly 15	CGC Arg	ATA Ile	GAC Asp	AAB Xaa	GTC Val 20	GAT Asp	GCT Ala	TTC Phe	ATG Met	AAC Asn 25	ATC Ile	321
				GTC Val										Val		369
				TTT Phe												417
	GAT Asp 60															423

(2) INFORMATION FOR SEQ ID NO: 188: (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 343 base pairs (B) TYPE: NUCLEIC ACID (C) STRANDEDNESS: DOUBLE (D) TOPOLOGY: LINEAR (ii) MOLECULE TYPE: CDNA (vi) ORIGINAL SOURCE: (A) ORGANISM: Homo Sapiens (F) TISSUE TYPE: Brain (ix) FEATURE: (A) NAME/KEY: other (B) LOCATION: 165..302 (C) IDENTIFICATION METHOD: blastn (D) OTHER INFORMATION: identity 93 region 33..170 id T50032 est (ix) FEATURE: (A) NAME/KEY: other (3) LOCATION: 291..339 (C) IDENTIFICATION METHOD: blastn (D) OTHER INFORMATION: identity 97 region 160..208 id T50032 est (ix) FEATURE: (A) NAME/KEY: other (B) LOCATION: 132..172 (C) IDENTIFICATION METHOD: blastn (D) OTHER INFORMATION: identity 97 region 1..41 id T50032 est (ix) FEATURE: (A) NAME/KEY: sig\_peptide (3) LOCATION: 71..139 (C) IDENTIFICATION METHOD: Von Heijne matrix (D) OTHER INFORMATION: score 4.4 seq QFILLGTTSVVTA/AL (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 188: AAGGTGGAGA SICSGGGGTC ACCAGGCCTA TCCTTGGCGC CACAGTCGGC CACCGGGGCT 60 CGCCGCCGTC ATB GAG AGC GGA GGG CGG CCC TCG CTG TGC CAG TTC ATC 109 Met Glu Ser Gly Gly Arg Pro Ser Leu Cys Gln Phe Ile -20 -15 CTC CTG GGC ACC TCT GTG GTC ACC GCC GCC CTG TAC TCC GTG TAC Leu Leu Gly Thr Thr Ser Val Val Thr Ala Ala Leu Tyr Ser Val Tyr 157

1

CGG CAG AAG GCC CGG GTC TCC CAA GAG CTC AAG GGA GCT AAA AAA GTT 205 Arg Gln Lys Ala Arg Val Ser Gln Glu Leu Lys Gly Ala Lys Lys Val CAT TTG GGT GAA GAT TTA AAG AGT ATT CTT TCA GAA GCT CCA GGA AAA 253 His Leu Gly Glu Asp Leu Lys Ser Ile Leu Ser Glu Ala Pro Gly Lys 25 30 TGC GTG CCT TAT GCT GTT ATA GAA GGA GCT GTG CGG TCT GTT AAA GAA 301 Cys Val Pro Tyr Ala Val Ile Glu Gly Ala Val Arg Ser Val Lys Glu 40 45 ACG CTT AAC AGC CAG TTT GTG GAA AAC TGC AAN GGG GTC CGG 343 Thr Leu Asn Ser Gln Phe Val Glu Asn Cys Xaa Gly Val Arg 55 60 65

#### (2) INFORMATION FOR SEQ ID NO: 189:

- (i) SEQUENCE CHARACTERISTICS:
  - (A) LENGTH: 481 base pairs
  - (B) TYPE: NUCLEIC ACID
  - (C) STRANDEDNESS: DOUBLE
  - (D) TOPOLOGY: LINEAR
- (ii) MOLECULE TYPE: CDNA
- (vi) ORIGINAL SOURCE:
  - (A) ORGANISM: Homo Sapiens
  - (F) TISSUE TYPE: Brain
- (ix) FEATURE:
  - (A) NAME/KEY: other
  - (B) LOCATION: 133..355
  - (C) IDENTIFICATION METHOD: blastn
  - (D) OTHER INFORMATION: identity 96 region 3..225 id H10707

est

- (ix) FEATURE:
  - (A) NAME/KEY: other
  - (B) LOCATION: 353..482
  - (C) IDENTIFICATION METHOD: blastn (D) OTHER INFORMATION: identity 97
    - region 224..353

id H10707

- (ix) FEATURE:
  - (A) NAME/KEY: other
  - (B) LOCATION: 154..354
  - (C) IDENTIFICATION METHOD: blastn
  - (D) OTHER INFORMATION: identity 93

region 98..298

id H30624

est

(ix) FEATURE:

(A) NAME/KEY: other (B) LOCATION: 36S..403 (C) IDENTIFICATION METHOD: blastn (D) OTHER INFORMATION: identity 94 region 314..349 id H30624

#### (ix) FEATURE:

- (A) NAME/KEY: other (B) LOCATION: 200..354
- (C) IDENTIFICATION METHOD: blastn
- (D) OTHER INFORMATION: identity 94 region 150..304 id HSC1VG011

est

est

#### (ix) FEATURE:

- (A) NAME/KEY: other
- (B) LOCATION: 111..198
- (C) IDENTIFICATION METHOD: blastn
- (D) OTHER INFORMATION: identity 92

region 62..149 id HSC1VG011

est

# (ix) FEATURE:

- (A) NAME/KEY: other
- (B) LOCATION: 49..85
- (C) IDENTIFICATION METHOD: blastn
- (D) OTHER INFORMATION: identity 97

region 1..37 id HSC1VG011

#### (ix) FEATURE:

- (A) NAME/KEY: other
- (B) LOCATION: 202..344
- (C) IDENTIFICATION METHOD: blastn
- (D) OTHER INFORMATION: identity 97

region 113..255

id R34406

est

# (ix) FEATURE:

- (A) NAME/KEY: other
- (B) LOCATION: 111..198
- (C) IDENTIFICATION METHOD: blastn
- (D) OTHER INFORMATION: identity 94

region 23..110 id R34406

#### (ix) FEATURE:

- (A) NAME/KEY: other
- (B) LOCATION: 353..482
- (C) IDENTIFICATION METHOD: blastn
- (D) OTHER INFORMATION: identity 99 region 115..244 id HSC23C111

est

(ix) FEATURE: (A) NAME/KEY: other (B) LOCATION: 240..355 (C) IDENTIFICATION METHOD: blastn (D) OTHER INFORMATION: identity 94 region 1..116 id HSC23C111 (ix) FEATURE: (A) NAME/KEY: sig peptide (B) LOCATION: 56..472 (C) IDENTIFICATION METHOD: Von Heijne matrix (D) OTHER INFORMATION: score 4.3 seq GILVPHSLRQAQA/SF (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 189: AAAAACTGCG GAGGGTGACA AGGAAGAAGG TGGCTCCAGA TCTGGAGGTG TGTCC ATG 58 Met GCG GCG CTT GAC CTG CGA GCG GAS TGG ATT CGC TGG TCC TGC AGC TGC 106 Ala Ala Leu Asp Leu Arg Ala Xaa Trp Ile Arg Trp Ser Cys Ser Cys -135 -130 TTG GGG GAM CTG GRA GGA GCT GGA GGG GAA ACG AAC GGT GTT GAA CGC 154 Leu Gly Xaa Leu Xaa Gly Ala Gly Gly Glu Thr Asn Gly Val Glu Arg -120 CCG GGT GGA GGG CTG GCT CTC GCT CGC CAA GGC TCG CTA CGC GAT 202 Pro Gly Gly Gly Leu Ala Leu Ala Arg Gln Gly Ser Leu Arg Asp -105 GGG CGC CAA GTC GGT AGG GCC CCT GCA GTA TGC TTC CCA CAT GGA GCC 250 Gly Arg Gln Val Gly Arg Ala Pro Ala Val Cys Phe Pro His Gly Ala -90 -85 CCA GGT CTG CCT CCA CGC CAG CGA GDC YCA GGA GGG DST CCA GAA GTT Pro Gly Leu Pro Pro Arg Gln Arg Xaa Xaa Gly Gly Xaa Pro Glu Val -70 CAA GGT GGT GAG AGC TGG TGT CCA CGC CCC AGA GGA GGT GGG GCC TCG Gln Gly Gly Glu Ser Trp Cys Pro Arg Pro Arg Gly Gly Gly Ala Ser -55 CGA ACA GGT CTG CGG AGG CGC AAG GGC CCC ACT AAG ACC CCA GAA CCG Arg Thr Gly Leu Arg Arg Lys Gly Pro Thr Lys Thr Pro Glu Pro -40 GAG TCC TCT GAG GCC CCT CAG GAC CCC CTG AAC TGG TTT GGA ATC CTA 442 Glu Ser Ser Glu Ala Pro Gln Asp Pro Leu Asn Trp Phe Gly Ile Leu -20 GTT CCT CAC AGT CTA CGT CAG GCT CAA GCA AGC TTC CGG

Val Pro His Ser Leu Arg Gln Ala Gln Ala Ser Phe Arg

-5

481

(2) INFORMATION FOR SEQ ID NO: 190:	
(i) SEQUENCE CHARACTERISTICS:  (A) LENGTH: 302 base pairs  (B) TYPE: NUCLEIC ACID  (C) STRANDEDNESS: DOUBLE  (D) TOPOLOGY: LINEAR	
(ii) MOLECULE TYPE: CDNA	
<ul><li>(vi) ORIGINAL SOURCE:</li><li>(Λ) ORGANISM: Homo Sapiens</li><li>(F) TISSUE TYPE: Brain</li></ul>	
<pre>(ix) FEATURE:     (A) NAME/KEY: other     (B) LOCATION: 176275     (C) IDENTIFICATION METHOD: blastn     (D) OTHER INFORMATION: identity 100</pre>	
(ix) FEATURE:  (A) NAME/KEY: sig_peptide  (B) LOCATION: 216278  (C) IDENTIFICATION METHOD: Von Heijne matrix  (D) OTHER INFORMATION: score 4.1  seq WWISLLPSLLSIC/KV	
(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 190:	
AAGCTTTCCC CGTGGTCTGA GTTTGTGGCT GCATTTTTAT CTCTGGTGGC TCTGCTACGG	60
CGGCGCAGAA ATGAGGCAGA AGCGGAAAGG AGATCTCAGC CCTGCTGAGC TGATGATGCT	120
GACTATAGGA GATGTTATTA AACAACTGAT TGAAGCCCAC GAGCAGGGGA AAGACATCGA	180
TCTAAATAAG GTGAAAACCA AGACAGCTGC CAAAT ATG GCC TTT CTG CCC AGC Met Ala Phe Leu Pro Ser -20	233
CCC GCC TGG TGG ATA TCA TTG CTG CCG TCC CTC AGT ATC TGC AAG Pro Ala Trp Trp Ile Ser Leu Leu Pro Ser Leu Leu Ser Ile Cys Lys -10 -15	281
GTC TTG ATG CCC AAG TTA AAG Val Leu Met Pro Lys Leu Lys 5	302
(2) INFORMATION FOR SEQ ID NO: 191:	
(1) SEQUENCE CHARACTERISTICS:  (A) LENGTH: 414 base pairs  (B) TYPE: NUCLEIC ACID  (C) STRANDEDNESS: DOUBLE  (D) TOPOLOGY: LINEAR	

WO 99/065	<b>352</b> 166	PCT/IB98/01		
(ii)	MOLECULE TYPE: CDNA			
(vi)	ORIGINAL SOURCE: (A) ORGANISM: Homo Sapiens (F) TISSUE TYPE: Brain			
(ix)	FEATURE: (A) NAME/KEY: other (B) LOCATION: 40271 (C) IDENTIFICATION METHOD: blastn (D) OTHER INFORMATION: identity 97 region 1232 id R00384 est			
(ix)	FEATURE: (A) NAME/KEY: other (B) LOCATION: 294328 (C) IDENTIFICATION METHOD: blastn (D) OTHER INFORMATION: identity 94 region 257291 id R00384 est	·		
(ix)	FEATURE: (A) NAME/KEY: other (B) LOCATION: 86130 (C) IDENTIFICATION METHOD: blastn (D) OTHER INFORMATION: identity 93 region 140184 id MMTEST284 est			
. '	FEATURE:  (A) NAME/KEY: sig_peptide  (B) LOCATION: 34180  (C) IDENTIFICATION METHOD: Von Heijne matrix  (D) OTHER INFORMATION: score 3.8  seq PAFHLPLPGPTLA/FL  SEQUENCE DESCRIPTION: SEQ ID NO: 191:			
AATTCCCCA	G CAAGCTCAGC GTGTAMSTGC GCT ATG GAG CCG AAA GTC GCA Met Glu Pro Lys Val Ala -45			
Leu Lys G	AG AAG ATC GAG GAC ACG CTA TGT CCT TTT GGC TTC GAG ( ln Lys Ile Glu Asp Thr Leu Cys Pro Phe Gly Phe Glu v 40 -35 -30			
	TC CAG GTG GCA TGG TAC AAT GAA CTC TTG CCT CCA GCC the Gln Val Ala Trp Tyr Asn Glu Leu Leu Pro Pro Ala -20 -15			
	CG CTG CCA GGA CCT ACC CTG GCC TTC CTG GTA CTC AGC Pro Leu Pro Gly Pro Thr Leu Ala Phe Leu Val Leu Ser			

CCT GCC ATG TTT GAC CGG GCC CTC AAG CCC TTC TTG CAG AGC TGC CAC Pro Ala Met Phe Asp Arg Ala Leu Lys Pro Phe Leu Gln Ser Cys His

<b>WO 99/06552</b>		<b>167</b>	20	PCT/IB98/01236
CTC CGA ATG CTG ACT Leu Arg Met Leu Thr 25	GAC CCA GTG Asp Pro Val	Asp Gln Cys	GTG GCC TAC CAT Val Ala Tyr His 35	CTG 294 Leu
GGC CGT GTT AGA GAG Gly Arg Val Arg Glu 40	AGC CTC CCA Ser Leu Pro 45	GAG CTG CAG Glu Leu Gln	ATA GAA ATC ATT Ile Glu Ile Ile 50	GCT 342 Ala
GRA HMA CGA GGT GCA Xaa Xaa Arg Gly Ala 55	CCC CAA CCG Pro Gln Pro 60	ACG CCC CAA Thr Pro Gln . 65	GAT CCT GGC CCA Asp Pro Gly Pro	GAC 390 Asp 70
AGC AGC CAT GTA GCT Ser Ser His Val Ala 75				414

# (2) INFORMATION FOR SEQ ID NO: 192:

- (i) SEQUENCE CHARACTERISTICS:
  - (A) LENGTH: 400 base pairs
  - (B) TYPE: NUCLEIC ACID
  - (C) STRANDEDNESS: DOUBLE
  - (D) TOPOLOGY: LINEAR
- (ii) MOLECULE TYPE: CDNA
- (vi) ORIGINAL SOURCE:
  - (A) ORGANISM: Homo Sapiens
  - (F) TISSUE TYPE: Brain
- (ix) FEATURE:
  - (A) NAME/KEY: other
  - (B) LOCATION: 324..389
  - (C) IDENTIFICATION METHOD: blastn
  - (D) OTHER INFORMATION: identity 95

region 301..366

id T08430

est

- (ix) FEATURE:
  - (A) NAME/KEY: other
  - (B) LOCATION: 64..400
  - (C) IDENTIFICATION METHOD: blastn
  - (D) OTHER INFORMATION: identity 90

region 1..337 id C17891

- (1%) FEATURE:
  - (A) NAME/KEY: other
  - (B) LOCATION: 301..400
  - (C) IDENTIFICATION METHOD: blastn
  - (D) OTHER INFORMATION: identity 95

region 1..100 id C04989

est

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1	$i \times 1$	FEATURE:

- (A) NAME/KEY: sig\_peptide
  (B) LOCATION: 107..145
- (C) IDENTIFICATION METHOD: Von Heijne matrix
- (D) OTHER INFORMATION: score 3.7

seq MLVLRSGLTKALA/SR

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 192:

AGAG	TTCG	CC F	GTGG	STCCA	G GA	GCCG	CTTI	TTT	CCAC	TCG	GGAA	GACT	TC P	AGAGA	AGTCT	60
CACA	AAGG	AC 1	rcggc	TGGC	T GC	TTTT	CTCA	GTG	CCGA	AGC	CGCC			CTC C Leu V		115
														GCG Ala 5		163
		Cys												GGA Gly		211
														AAT Asn		259
														TAC Tyr		307
														AAT Asn	AAA Lys 70	355
				Trp		Tyr	Asp	Asn	Phe	Ala	His	Arg	Ala	GAA Glu		400

# (2) INFORMATION FOR SEQ ID NO: 193:

- (i) SEQUENCE CHARACTERISTICS:
  - (A) LENGTH: 186 base pairs
  - (B) TYPE: NUCLEIC ACID
  - (C) STRANDEDNESS: DOUBLE
  - (D) TOPOLOGY: LINEAR
- (ii) MOLECULE TYPE: CDNA
- (vi) ORIGINAL SOURCE:
  - (A) ORGANISM: Homo Sapiens
  - (F) TISSUE TYPE: Brain
- (ix) FEATURE:
  - (A) NAME/KEY: other
  - (B) LOCATION: 112..184
  - (C) IDENTIFICATION METHOD: blastn
  - (D) OTHER INFORMATION: identity 98 region 1..73

id HSC09D101

(ix) FEATURE:

(A) NAME/KEY: other

(B) LOCATION: 112..184

(C) IDENTIFICATION METHOD: blastn

(D) OTHER INFORMATION: identity 98 region 1..73 id HSC2UE011

(ix) FEATURE:

(A) NAME/KEY: other (B) LOCATION: 112..186

(C) IDENTIFICATION METHOD: blastn

(D) OTHER INFORMATION: identity 90 region 1..75 id HSC09C101

(ix) FEATURE:

(A) NAME/KEY: other (B) LOCATION: 140..184

(C) IDENTIFICATION METHOD: blastn

(D) OTHER INFORMATION: identity 95 region 17..61 id T35421

(ix) FEATURE:

(A) NAME/KEY: sig\_peptide

(B) LOCATION: 106..174

(C) IDENTIFICATION METHOD: Von Heijne matrix

(D) OTHER INFORMATION: score 10.5

seq LLFVLLLFSLLPA/CL

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 193:

ATATTTAAAC GACCCTTCAA AGGCCCTTAG GTTTCCTTGC CTCTGCTCAC AGAACTAGTC

CAGCCAGGTG TCGCTGCTGC CTCAGAGCTG TGTGGGGTCG CRTGT ATG TCG GGG GGC 117 Met Ser Gly Gly

-20

CAT CTT GCC GAT TTA ACG CTG CTT TTT GTG TTG TTG TTT TCC CTC His Leu Ala Asp Leu Thr Leu Leu Phe Val Leu Leu Phe Ser Leu

-10

CTC CCT GCC TGC CTA CCC CGG Leu Pro Ala Cys Leu Pro Arg 7

186

(2) INFORMATION FOR SEQ ID NO: 194:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 335 base pairs

(B) TYPE: NUCLEIC ACID

- (C) STRANDEDNESS: DOUBLE
- (D) TOPOLOGY: LINEAR
- (ii) MOLECULE TYPE: CDNA
- (vi) ORIGINAL SOURCE:
  - (A) ORGANISM: Homo Sapiens
  - (F) TISSUE TYPE: Brain
- (ix) FEATURE:
  - (A) NAME/KEY: other
  - (B) LOCATION: complement (86..336)
  - (C) IDENTIFICATION METHOD: blastn
  - (D) OTHER INFORMATION: identity 99

region 79..329 id AA148596

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est

- (ix) FEATURE:
  - (A) NAME/KEY: other
  - (B) LOCATION: complement (30..91)
  - (C) IDENTIFICATION METHOD: blastn
  - (D) OTHER INFORMATION: identity 100

region 325..386

id AA148596

est

- (ix) FEATURE:
  - (A) NAME/KEY: other
  - (B) LOCATION: complement (2..39)
  - (C) IDENTIFICATION METHOD: blastn
  - (D) OTHER INFORMATION: identity 92

region 378..415

id AA148596

est

- (ix) FEATURE:
  - (A) NAME/KEY: other
  - (B) LOCATION: complement(2..336)
  - (C) IDENTIFICATION METHOD: blastn
  - (D) OTHER INFORMATION: identity 99

region 67..401 id AA074631

est

- (ix) FEATURE:
  - (A) NAME/KEY: other
  - (B) LOCATION: complement(83..336)
  - (C) IDENTIFICATION METHOD: blastn
  - (D) OTHER INFORMATION: identity 99

region 64..317

id AA078818

est

- (ix) FEATURE:
  - (A) NAME/KEY: other
  - (B) LOCATION: complement (8..48)
  - (C) IDENTIFICATION METHOD: blastn
  - (D) OTHER INFORMATION: identity 97

region 355..395

id AA078818

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est

(ix) FEATURE:

(A) NAME/KEY: other (B) LOCATION: complement(30336) (C) IDENTIFICATION METHOD: blastn (D) OTHER INFORMATION: identity 99 region 64370 id N21054 est	
(ix) FEATURE:  (A) NAME/KEY: other  (B) LOCATION: complement(68236)  (C) IDENTIFICATION METHOD: blastn  (D) OTHER INFORMATION: identity 98  region 172340  id AA157994  est	
<pre>(ix) FEATURE:     (A) NAME/KEY: other     (B) LOCATION: complement(225336)     (C) IDENTIFICATION METHOD: blastn     (D) OTHER INFORMATION: identity 94</pre>	
(ix) FEATURE:  (A) NAME/KEY: other  (B) LOCATION: complement(2868)  (C) IDENTIFICATION METHOD: blastn  (D) OTHER INFORMATION: identity 100  region 341381  id AA157994  est	
<pre>(ix) FEATURE:     (A) NAME/KEY: sig_peptide     (B) LOCATION: 174326     (C) IDENTIFICATION METHOD: Von Heijne matrix     (D) OTHER INFORMATION: score 10.1</pre>	
(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 194:	
AATTCTCAAC GAGCTGCGGG CTCGGCATGC CCAGGGGGGT ACATGGTATG GAGTAGACAT	60
CAACAACGAG GACATTGCTG ACAACTTTGA AGCTTTCGTG TGGGAGCCAG CTATGGTGCG	120
GATCAATGCG CTGACAGCAG CCTCTGAGGC TGCGTGCCTG ATCGTGTCTG TAG ATG	176
-50 -45 -40 -35	224
GCC GGG GCC GTG GTC GTG GCC GCC CCC ACT GAG AGG CAC CCC ACC CAT Ala Gly Ala Val Val Ala Ala Pro Thr Glu Arg His Pro Thr His	272

-25

CAC ATG GCT GGC TGG CTG GGT GCA CTT ACC CTC CTT GGC TTG GTT
His Met Ala Gly Trp Leu Leu Gly Ala Leu Thr Leu Leu Gly Leu Val

-15 -10 -5

ACT TCA TTT TAC AAG Thr Ser Phe Tyr Lys 335

-20

# (2) INFORMATION FOR SEQ ID NO: 195:

-30

- (i) SEQUENCE CHARACTERISTICS:
  - (A) LENGTH: 419 base pairs
  - (B) TYPE: NUCLEIC ACID
  - (C) STRANDEDNESS: DOUBLE
  - (D) TOPOLOGY: LINEAR
- (ii) MOLECULE TYPE: CDNA
- (vi) ORIGINAL SOURCE:
  - (A) ORGANISM: Homo Sapiens
  - (F) TISSUE TYPE: Brain
- (ix) FEATURE:
  - (A) NAME/KEY: other
  - (B) LOCATION: 23..200
  - (C) IDENTIFICATION METHOD: blastn
  - (D) OTHER INFORMATION: identity 100 region 9..186 id W44639

est

- (ix) FEATURE:
  - (A) NAME/KEY: other
  - (B) LOCATION: 216..356
  - (C) IDENTIFICATION METHOD: blastn
  - (D) OTHER INFORMATION: identity 99 region 200..340

id W44639 est

- (ix) FEATURE:
  - (A) NAME/KEY: other
  - (B) LOCATION: 363..412
  - (C) IDENTIFICATION METHOD: blastn
  - (D) OTHER INFORMATION: identity 100

region 347..396

id W44639

est

- (ix) FEATURE:
  - (A) NAME/KEY: sig\_peptide
  - (B) LOCATION: 27..218
  - (C) IDENTIFICATION METHOD: Von Heijne matrix
  - (D) OTHER INFORMATION: score 9.5

seq LSLLAALAHLAAA/EK

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 195:

AGTO	SGGTC	IGA E	CTGC	GGCC	GC AC	STCGO			e Pro		GCC A Ala	53
					CAG Gln -50							101
					GAC Asp							149
					GCG Ala							197
					GCG Ala							245
					GGG Gly 15							293
					ACT Thr							341
					DDK Xaa							389
					AGA Arg							419

# (2) INFORMATION FOR SEQ ID NO: 196:

- (i) SEQUENCE CHARACTERISTICS:
  - (A) LENGTH: 342 base pairs
  - (B) TYPE: NUCLEIC ACID
  - (C) STRANDEDNESS: DOUBLE
  - (D) TOPOLOGY: LINEAR
- (ii) MOLECULE TYPE: CDNA
- (vi) ORIGINAL SOURCE:
  - (A) ORGANISM: Homo Sapiens
  - (F) TISSUE TYPE: Brain
- (12) FEATURE:

  - (A) NAME/KEY: other
    (B) LOCATION: 33..269
    (C) IDENTIFICATION METHOD: blastn
  - (D) OTHER INFORMATION: identity 99 region 10..246 id AA058587

est

(ix) FEATURE:

(A) NAME/KEY: other (B) LOCATION: 272..307

(C) IDENTIFICATION METHOD: blastn

(D) OTHER INFORMATION: identity 100

region 249..283

id AA058587

est

(ix) FEATURE:

(A) NAME/KEY: other
(B) LOCATION: 133..259

(C) IDENTIFICATION METHOD: blastn

(D) OTHER INFORMATION: identity 100

region 87..213

id R12128

est

(ix) FEATURE:

(A) NAME/KEY: other (B) LOCATION: 47..134

(C) IDENTIFICATION METHOD: blastn

(D) OTHER INFORMATION: identity 98

region 2..89 id R12128

est

(ix) FEATURE:

(A) NAME/KEY: other

(B) LOCATION: 303..337

(C) IDENTIFICATION METHOD: blastn

(D) OTHER INFORMATION: identity 97

region 257..291

id R12128

est

(ix) FEATURE:

(A) NAME/KEY: other

(B) LOCATION: 49..259

(C) IDENTIFICATION METHOD: blastn

(D) OTHER INFORMATION: identity 98

region 2..212

id H19999

est

(ix) FEATURE:

(A) NAME/KEY: other

(B) LOCATION: 272..304

(C) IDENTIFICATION METHOD: blastn

(D) OTHER INFORMATION: identity 96

region 225..257

id H19999

est

(ix) FEATURE:

(A) NAME/KEY: other
(B) LOCATION: 303..337

(C) IDENTIFICATION METHOD: blastn

(D) OTHER INFORMATION: identity 91

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175 region 257..291 ıd H19999 est (ix) FEATURE: (A) NAME/KEY: other (B) LOCATION: 42..252 (C) IDENTIFICATION METHOD: blastn (D) OTHER INFORMATION: identity 99 region 1..211 id R20025 est (ix) FEATURE: (A) NAME/KEY: other (B) LOCATION: 87..259 (C) IDENTIFICATION METHOD: blastn (D) OTHER INFORMATION: identity 99 region 1..173 id H83838 est (ix) FEATURE: (A) NAME/KEY: other (B) LOCATION: 272..337 (C) IDENTIFICATION METHOD: blastn (D) OTHER INFORMATION: identity 98 region 186..251 id H83838 (ix) FEATURE: (A) NAME/KEY: sig\_peptide (B) LOCATION: 85..198 (C) IDENTIFICATION METHOD: Von Heijne matrix (D) OTHER INFORMATION: score 9.3 seq QLLYLSLLSGLHG/QE (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 196: AGGCTGCGGT AAATCCGGGC TTGCGGCCGC TGGCGTAGTC TGTGGCCGGG TGGTCGTTGC TGCGCGCCCC GAGCCCCGAG AGCC ATG CAG ATG TCC TAC GCC ATC CGG TGC 111 Met Gln Met Ser Tyr Ala Ile Arg Cys -35 GCC TTC TAC CAG CTG CTG GCC GCG CTC ATG CTG GCG ATG CTG 159 Ala Phe Tyr Gln Leu Leu Leu Ala Ala Leu Met Leu Val Ala Met Leu -20 CAG CTG CTC TAC CTG TCG CTG TCC GGA CTG CAC GGG CAG GAG GAG 207 Gln Leu Leu Tyr Leu Ser Leu Leu Ser Gly Leu His Gly Gln Glu -10 CAA GAC CAA TAT TIT GAG TIC TIT CCC CCG TOU CCA CGG TCC GIG GAC Gln Asp Gln Tyr Phe Glu Phe Phe Pro Pro Ser Pro Arg Ser Val Asp

10

CAG GTC AAG GCT CAG CTC CGC ACC GCG CTG GTT TOT GGA GGC GTD CTG

Gln Val Lys Ala Gln Les Ary Thr Ala Leu A a Ser Gly Gly V. Leu

303

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35

342

GAC GCT AGC GGC GAT TAC CGC GTC TAC AGG GGC CAT GGG
Asp Ala Ser Gly Asp Tyr Arg Val Tyr Arg Gly His Gly
40
45

(2) INFORMATION FOR SEQ ID NO: 197:

- (i) SEQUENCE CHARACTERISTICS:
  - (A) LENGTH: 461 base pairs
  - (B) TYPE: NUCLEIC ACID
  - (C) STRANDEDNESS: DOUBLE
  - (D) TOPOLOGY: LINEAR
- (ii) MOLECULE TYPE: CDNA
- (vi) ORIGINAL SOURCE:
  - (A) ORGANISM: Homo Sapiens
  - (F) TISSUE TYPE: Brain
- (ix) FEATURE:
  - (A) NAME/KEY: other
  - (B) LOCATION: complement (149..337)
  - (C) IDENTIFICATION METHOD: blastn
  - (D) OTHER INFORMATION: identity 97 region 182..370 id AA142966

est

(ix) FEATURE:

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- (A) NAME/KEY: other
- (B) LOCATION: complement (340..459)
- (C) IDENTIFICATION METHOD: blastn
- (D) OTHER INFORMATION: identity 97 region 61..180 id AA142966

est

- (ix) FEATURE:
  - (A) NAME/KEY: other
  - (B) LOCATION: complement (142..337)
  - (C) IDENTIFICATION METHOD: blastn
  - (D) OTHER INFORMATION: identity 98 region 183..378

id AA019334

est

- (ix) FEATURE:
  - (A) NAME/KEY: other
  - (B) LOCATION: complement(340..459)
  - (C) IDENTIFICATION METHOD: blastn
  - (D) OTHER INFORMATION: identity 97 region 62..181

id AA019334

est

- (ix) FEATURE:
  - (A) NAME/KEY: other
  - (B) LOCATION: complement (345..459)

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> region 1..150 id 278830 est

177 (C) IDENTIFICATION METHOD: blastn (D) OTHER INFORMATION: identity 95 region 48..162 id N66447 est (ix) FEATURE: (A) NAME/KEY: other (B) LOCATION: complement(255..337) (C) IDENTIFICATION METHOD: blastn (D) OTHER INFORMATION: identity 97 region 170..252 id N66447 est (ix) FEATURE: (A) NAME/KEY: other (B) LOCATION: complement (111..181) (C) IDENTIFICATION METHOD: blastn (D) OTHER INFORMATION: identity 95 region 330..400 id N66447 est (ix) FEATURE: (A) NAME/KEY: other (B) LOCATION: complement (179..228) (C) IDENTIFICATION METHOD: blastn (D) OTHER INFORMATION: identity 98 region 282..331 id N66447 est (ix) FEATURE: (A) NAME/KEY: other (B) LOCATION: complement(172..337) (C) IDENTIFICATION METHOD: blastn (D) OTHER INFORMATION: identity 97 region 113..278 id R85770 est (ix) FEATURE: (A) NAME/KEY: other (B) LOCATION: complement(340..450) (C) IDENTIFICATION METHOD: blastn (D) OTHER INFORMATION: identity 98 region 1..111 id R85770 est (1K) FEATURE: (A) NAME/KEY: other (B) LOCATION: 188..337 (C) IDENTIFICATION METHOD: blastn (D) OTHER INFORMATION: identity 99

1/6	
(A) NAME/KEY: other (B) LOCATION: 339459 (C) IDENTIFICATION METHOD: blastn (D) OTHER INFORMATION: identity 96 region 151271 id R78830 est	
<pre>(ix) FEATURE:     (A) NAME/KEY: sig_peptide     (B) LOCATION: 384455     (C) IDENTIFICATION METHOD: Von Heijne matrix     (D) OTHER INFORMATION: score 9.1</pre>	·
(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 197:	
AACACTGTTG TATAAACTAA TCTTTGCTTG TTTTCTACTC TGTGATCTTT CCATATCATA	60
TTTCATTAAT GATCAGTTAG TGTCAAGGAG TCAAAACAGA TTAAAATTAA TTTCATGTGT	120
ATATGGTGGA AATTTGTGGC TAGTGTGATT TTTGTTTGTY TCCTTTTAAG TACTGTTGAT	180
CAGTTGTGAC ACTTACTGGT TAAACTTACG TTGCTAAAGA TTTCTCTATA ATAAGCCACA	240
CATTATATTT AGACTATATT AAGGGACCTT GGTTTTCTTC TAGATAGCAG CTGTCCCAAA	300
GAAAATATTT CTTCTTTGTC TGTKAAGATT TAGCTATNKA TCTGCCAGTT GTTCAGMGGT	360
TTTGGTTCCA AACTCAACCA GCA ATG TTG AGA GCT GAA CTT AAG ATA GCT GTT  Met Leu Arg Ala Glu Leu Lys Ile Ala Val  -20 -15	413
GTA CTT TTT GCT TTC CAT CTG TTA CTG TCC TTC ATT CTC GGC TCC CGG Val Leu Phe Ala Phe His Leu Leu Ser Phe Ile Leu Gly Ser Arg -10 -5 1	461
(2) INFORMATION FOR SEQ ID NO: 198:	
<ul> <li>(i) SEQUENCE CHARACTERISTICS:</li> <li>(A) LENGTH: 229 base pairs</li> <li>(B) TYPE: NUCLEIC ACID</li> <li>(C) STRANDEDNESS: DOUBLE</li> <li>(D) TOPOLOGY: LINEAR</li> </ul>	
(ii) MOLECULE TYPE: CDNA	
<pre>(vi) ORIGINAL SOURCE:    (A) ORGANISM: Homo Sapiens    (F) TISSUE TYPE: Brain</pre>	
(ix) FEATURE:	

(A) NAME/KEY: other

(B) LOCATION: complement(1..130)
(C) IDENTIFICATION METHOD: blastn

(D) OTHER INFORMATION: identity 98 region 8..137 id H63707

	est
:	D: Von Heijne matrix score 9 seq LLILLLRTFLCSA/MI
(xi) SEQUENCE DESCRIPTION: SEQ	ID NO: 198:
A ATG AAT CAT CAA CAG ACA TTA ATT GGC Met Asn His Gln Gln Thr Leu Ile Gly -55	Alg Leu Leu Cys Asp Leu His
	ish Ash Val Gln Ala Leu Phe 30 —25
AGA ATG CTT ACT CCT GAA GCT TAT TCC T Arg Met Leu Thr Pro Glu Ala Tyr Ser C -20	ys Leu Leu Ile Leu Leu -10
AGG ACT TTT CTG TGT AGT GCA ATG ATA GATA G	CA AAT ACA CTT CAT CTC AAG 193 la Asn Thr Leu Eis Leu Lys 5
TAC CAT CTC CAA TTG ATT GAT AAT GCC TO Tyr His Leu Gln Leu Ile Asp Asn Ala Cy 10	GC CCT GAG ys Pro Glu 20
(2) INFORMATION FOR SEQ ID NO: 199:  (i) SEQUENCE CHARACTERISTICS:  (A) LENGTH: 278 base pairs  (B) TYPE: NUCLEIC ACID  (C) STRANDEDNESS: DOUBLE  (D) TOPOLOGY: LINEAR	
(ii) MOLECULE TYPE: CDNA	

- (vi) ORIGINAL SOURCE:
  - (A) ORGANISM: Homo Sapiens
  - (F) TISSUE TYPE: Brain
- (ix) FEATURE:
  - (A) NAME/KEY: other
  - (B) LOCATION: 145..279
  - (C) IDENTIFICATION METHOD: blastn
  - (D) OTHER INFORMATION: identity 100 region 1..135 id H06014 est
- (ix) FEATURE:
  - (A) NAME/KEY: other (B) LOCATION: 180..279
  - (C) IDENTIFICATION METHOD: blastn

(D) OTHER INFORMATION: i

identity 100 region 11..110

id R15960

est

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(A) NAME/KEY: other

(B) LOCATION: 204..279

(C) IDENTIFICATION METHOD: blastn
(D) OTHER INFORMATION: identity 96

region 1..76

id W67034

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# (ix) FEATURE:

(A) NAME/KEY: sig\_peptide

(B) LOCATION: 27..146

(C) IDENTIFICATION METHOD: Von Heijne matrix

(D) OTHER INFORMATION: score 8.6

seq LFCVLGIVLLVTG/IV

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 199:

ACCAAACCAA AGCCGTCATC ATTGCA ATG ATC ATC ACT GCG GTG GTA TCC ATT

Met Ile Ile Thr Ala Val Val Ser Ile

-40

TCA GTC ACC ATC TTC TGC TTT CAG ACC AAG GTG GAC TTC ACC TCG TGC

Ser Val Thr Ile Phe Cys Phe Gln Thr Lys Val Asp Phe Thr Ser Cys

-30

-25

-20

ACA GGC CTC TTC TGT GTC CTG GGA ATT GTG CTC CTG GTG ACT GGG ATT

Thr Gly Leu Phe Cys Val Leu Gly Ile Val Leu Leu Val Thr Gly Ile

-15

-10

-5

149

GTC ACT AGC ATT GTG CTC TAC TTC CAA TAC GTT TAC TGG CTC CAC ATG

Val Thr Ser Ile Val Leu Tyr Phe Gln Tyr Val Tyr Trp Leu His Met

5

10

CTC TAT GCT GCT CTG GGG GCC ATT TGT TTC ACC CTG TTC CTG GCT TAC

Leu Tyr Ala Ala Leu Gly Ala Ile Cys Phe Thr Leu Phe Leu Ala Tyr

20 25 30

GAC ACA CAG CTG GTC CTG GGG AAC CGG AAG CAC
Asp Thr Gln Leu Val Leu Gly Asn Arg Lys His
35
40

# (2) INFORMATION FOR SEQ ID NO: 200:

# (i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 333 base pairs
- (B) TYPE: NUCLEIC ACID
- (C) STRANDEDNESS: DOUBLE
- (D) TOPOLOGY: LINEAR
- (ii) MOLECULE TYPE: CDNA
- (vi) ORIGINAL SOURCE:

(A) ORGANISM: Homo Sapiens (F) TISSUE TYPE: Brain (ix) FEATURE: (A) NAME/KEY: other (B) LOCATION: 55..268 (C) IDENTIFICATION METHOD: blastn (D) OTHER INFORMATION: identity 95 region 32..245 id T60555 est (ix) FEATURE: (A) NAME/KEY: other (B) LOCATION: 22..51 (C) IDENTIFICATION METHOD: blastn (D) OTHER INFORMATION: identity 90 region 1..30 id T60555 (ix) FEATURE: (A) NAME/KEY: sig\_peptide (B) LOCATION: 67..261 (C) IDENTIFICATION METHOD: Von Heijne matrix (D) OTHER INFORMATION: score 8.4 sed LLWFIHLVFVVLX/LF (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 200: AAGAGGCTTA CGAGSWCCAG GTGGAGAGGC CGGGCTGGCC AAGGCTTCGG CCTCCGGCGT 60 CGGGAA ATG GCG GCG GGC AGG ATG GAG GAC GGT TCC TTG GAT ATC Met Ala Ala Gly Gly Arg Met Glu Asp Gly Ser Leu Asp Ile 108 -60 ACC CAG AGT ATT GAA GAC GAC CCA CTT CTG GAT GCC CAG CTT CTC CCA Thr Gln Ser Ile Glu Asp Asp Pro Leu Leu Asp Ala Gln Leu Leu Pro 156 -40CAC CAC TCA TTA CAA GCT CAC TTT AGA CCC CGA TTC CAT CCT CCT His His Ser Leu Gln Ala His Phe Arg Pro Arg Phe His Pro Leu Pro 204 -25 ACA GTC ATA GTG AAT CTT CTG TGG TTT ATT CAT CTC GTG TTT GTT Thr Val Ile Ile Val Asn Leu Leu Trp Phe Ile His Leu Val Phe Val 252 -10 GTW TTA GSA TTG TTT AAC AGG TGT GCT TTG TTC TWA TCC TAT CCC AAA Val Leu Xaa Leu Phe Asn Arg Cys Ala Leu Phe Xaa Ser Tyr Pro Lys

333

(2) INFORMATION FOR SEQ ID NO: 201:

15

TGG GAC ARG TGC CCA GGA AAT TAC ACA AAC CCA Trp Asp Xaa Cys Pro Gly Asn Tyr Thr Asn Pro

20

(i) SEQUENCE CHARACTERISTICS:  (A) LENGTH: 337 base pairs  (B) TYPE: NUCLEIC ACID  (C) STRANDEDNESS: DOUBLE  (D) TOPOLOGY: LINEAR	
(ii) MOLECULE TYPE: CDNA	
<pre>(vi) ORIGINAL SOURCE:     (A) ORGANISM: Homo Sapiens     (F) TISSUE TYPE: Brain</pre>	
(ix) FEATURE:  (A) NAME/KEY: other  (B) LOCATION: 125306  (C) IDENTIFICATION METHOD: blastn  (D) OTHER INFORMATION: identity 95  region 95276  id H31193  est	
(ix) FEATURE:  (A) NAME/KEY: other  (B) LOCATION: 69130  (C) IDENTIFICATION METHOD: blastn  (D) OTHER INFORMATION: identity 93  region 40101  id H31193  est	
(ix) FEATURE:  (A) NAME/KEY: other  (B) LOCATION: 2968  (C) IDENTIFICATION METHOD: blastn  (D) OTHER INFORMATION: identity 97  region 140  id H31193  est	
<pre>(ix) FEATURE:     (A) NAME/KEY: sig_peptide     (B) LOCATION: 161208     (C) IDENTIFICATION METHOD: Von Heijne matrix     (D) OTHER INFORMATION: score 7.5</pre>	
(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 201:	
AATCGCTTGG GAGCTGCTGC AGGATGGAGT GGAAAGCTGC TGCTGATGGC ATTGTTTTTG 6	0
TGGCAGCAAG CTGAATGACA GATCCTCACT ACAAAGATAC CCCTTTGGCC CCCGTGTAGG 12	20
CCTCCTTGGT TCGGGTGTTT CACCATGCCA GCACAGCGCC ATG AGT CCT GGA TGC  Met Ser Pro Gly Cys -15	75
ATG CTG CTG TTT GTG TTT GGC TTT GTT GGC GGG GCG GTG GT	23

WO 99/06552 183 TCT GCT ATC TTA GTA TCT CTC TCT GTT TTG CTG CTT GTG CAC TTT TCT Ser Ala Ile Leu Val Ser Leu Ser Val Leu Leu Val His Phe Ser 20 ATT TCT ACC GGT GTG CCA GCT CTG ACG CAG AAC CTA CCA AGG ATA CTC Ile Ser Thr Gly Val Pro Ala Leu Thr Gln Asn Leu Pro Arg Ile Leu 319 30 AGA AAA GAA CGC CCC GGG Arg Lys Glu Arg Pro Gly 337 40 (2) INFORMATION FOR SEQ ID NO: 202: (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 309 base pairs (3) TYPE: NUCLEIC ACID (C) STRANDEDNESS: DOUBLE (D) TOPOLOGY: LINEAR (ii) MOLECULE TYPE: CDNA (vi) ORIGINAL SOURCE: (A) ORGANISM: Homo Sapiens (F) TISSUE TYPE: Brain (ix) FEATURE: (A) NAME/KEY: other (B) LOCATION: 105..252 (C) IDENTIFICATION METHOD: blastn (D) OTHER INFORMATION: identity 94 region 136..283 id HSU46355 est (ix) FEATURE:

- (A) NAME/KEY: other
- (B) LOCATION: 53..83
- (C) IDENTIFICATION METHOD: blastn
- (D) OTHER INFORMATION: identity 90

region 82..112 id HSU46355

# (ix) FEATURE:

- (A) NAME/KEY: other
- (3) LOCATION: 227..276
- (C) IDENTIFICATION METHOD: blastn
- (D) OTHER INFORMATION: identity 94

region 206..255 id AA011705 est

### (ix) FEATURE:

- (A) NAME/KEY: sig\_peptide
- (B) LOCATION: 109..153
- (C) IDENTIFICATION METHOD: Von Heijne matrix
- (3) OTHER INFORMATION: score 7.5 seq LLLGIALLAYVAS/VW

# (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 202:

AATBGTGCAG CAGGCGGGCC CCCGCGCGGC AGGGSCCTGG ACCCGCGCGG CTCCCTGGGA TGGTGAGCAA GGCGCTGCTG CSCTCGTGTC TGCCGTCAAC CGCAGASG ATG AAG CTG 1117 Met Lys Leu -15 CTG CTG GGC ATC GCC TTG CTG GCC TAC GTC GCC TCT GTT TGG GGC AAC 165 Leu Leu Gly Ile Ala Leu Leu Ala Tyr Val Ala Ser Val Trp Gly Asn -10 TTC GTT AAT ATG AGG TCT ATC CAG GAA AAT GGT GAA CTA AAA ATT GAA 213 Phe Val Asn Met Arg Ser Ile Gln Glu Asn Gly Glu Leu Lys Ile Glu 10 15 AGC AAG ATT GAA GAG ATG GTT GAA CCA CTA AGA GAG AAA ATC AGA GAT 261 Ser Lys Ile Glu Glu Met Val Glu Pro Leu Arg Glu Lys Ile Arg Asp. TTA GRA AAA AGC TTT ACC CAG AAA TAC CCA CCA GTA AAG TTT TTA TCA 309 Leu Xaa Lys Ser Phe Thr Gln Lys Tyr Pro Pro Val Lys Phe Leu Ser 40 45

### (2) INFORMATION FOR SEQ ID NO: 203:

- (i) SEQUENCE CHARACTERISTICS:
  - (A) LENGTH: 491 base pairs
  - (B) TYPE: NUCLEIC ACID
  - (C) STRANDEDNESS: DOUBLE
  - (D) TOPOLOGY: LINEAR
- (ii) MOLECULE TYPE: CDNA
- (vi) ORIGINAL SOURCE:
  - (A) ORGANISM: Homo Sapiens
  - (F) TISSUE TYPE: Brain
- (ix) FEATURE:
  - (A) NAME/KEY: other
  - (B) LOCATION: 132..251
  - (C) IDENTIFICATION METHOD: blastn
  - (D) OTHER INFORMATION: identity 99 region 170..289

id T60981

est

- (ix) FEATURE:
  - (A) NAME/KEY: other
  - (B) LOCATION: 19..126
  - (C) IDENTIFICATION METHOD: blastn
  - (D) OTHER INFORMATION: identity 99 region 57..164 id T60981

est

(ix) FEATURE:

#### PCT/IB98/01236 WO 99/06552 185

(A) NAME/KEY: sig_peptide (B) LOCATION: 39107 (C) IDENTIFICATION METHOD: Von Heijne matrix (D) OTHER INFORMATION: score 7.5 seq_LVLLLTLPLHLMA/LL (xi) SEQUENCE DESCRIPTION: SEQ_ID_NO: 203:														
AAGTGCCCCA GCGGAAGACA GCTCAGAGCT GGTCTGCC ATG GAC ATC CTG GTC CCA Met Asp Ile Leu Val Pro -20														
CTC CTG CAG CTG CTG GTG CTG CTT CTT ACC CTG CCC CTG CAC CTC ATG Leu Leu Gln Leu Leu Val Leu Leu Leu Thr Leu Pro Leu His Leu Met -15 -10 -5	104													
GCT CTG CTG GGC TGC TGG CAG CCC CTG TGC AAA AGC TAC TTC CCC TAC Ala Leu Leu Gly Cys Trp Gln Pro Leu Cys Lys Ser Tyr Phe Pro Tyr 1 5 10 15	152													
CTG ATG GCC GTG CTG ACT CCC AAG AGC AAC CGC AAG ATG GAG AGC AAG Leu Met Ala Val Leu Thr Pro Lys Ser Asn Arg Lys Met Glu Ser Lys 20 25 30	200													
AAA CGG GAG CTC TTC AGC CAG ATA AAG GGG CTT ACA GGA GCC TCC GGG Lys Arg Glu Leu Phe Ser Gln Ile Lys Gly Leu Thr Gly Ala Ser Gly 35 40 45	248													
AAA GTG GCC CTA CTG GAG CTG GGC TGC GGA ACC GGA GCC AAC TTT CAG Lys Val Ala Leu Leu Glu Leu Gly Cys Gly Thr Gly Ala Asn Phe Gln 50 55 60	296													
TTC TAC CCA CCG GGC TGC AGG GTC ACC TGC CTA GAC CCA AAT CCC CAC Phe Tyr Pro Pro Gly Cys Arg Val Thr Cys Leu Asp Pro Asn Pro His 65	344													
TTT GAG AAG TTC CTG ACA AAG AGC ATG GCT GAG AAC AGG CAC CTC CAA Phe Glu Lys Phe Leu Thr Lys Ser Met Ala Glu Asn Arg His Leu Gln 80 90 95	392													
TAT GAG CGG TTT GTG GTG GCT CCT GGA GAG GAC ATG AGA MAG CTG GCT Tyr Glu Arg Phe Val Val Ala Pro Gly Glu Asp Met Arg Xaa Leu Ala 100 105 110	440													
GAT GGC TCC ATG GAT GTK GTG GTC TGC ACT CTG GTG CTG TGC TCT GTG Asp Gly Ser Met Asp Val Val Val Cys Thr Leu Val Leu Cys Ser Val	488													
CAG Gln	491													

# (2) INFORMATION FOR SEQ ID NO: 204:

- (i) SEQUENCE CHARACTERISTICS:
  - (A) LENGTH: 331 base pairs

  - (B) TYPE: NUCLEIC ACID
    (C) STRANDEDNESS: DOUBLE
  - (D) TOPOLOGY: LINEAR

(ii) MOLECULE TYPE: CDNA

### (vi) ORIGINAL SOURCE:

- (A) ORGANISM: Homo Sapiens
- (F) TISSUE TYPE: Brain

### (ix) FEATURE:

- (A) NAME/KEY: other
- (B) LOCATION: 25..303
- (C) IDENTIFICATION METHOD: blastn
- (D) OTHER INFORMATION: identity 98 region 1..279

id HSC0ZA041

est

### (ix) FEATURE:

- (A) NAME/KEY: other
- (B) LOCATION: 131..286
- (C) IDENTIFICATION METHOD: blastn
- (D) OTHER INFORMATION: identity 97

region 106..261

id R12615

est

### (ix) FEATURE:

- (A) NAME/KEY: other
- (B) LOCATION: 71..133
- (C) IDENTIFICATION METHOD: blastn
- (D) OTHER INFORMATION: identity 100

region 47..109

id R12615

est

# (ix) FEATURE:

- (A) NAME/KEY: other
- (B) LOCATION: 88..303
- (C) IDENTIFICATION METHOD: blastn
- (D) OTHER INFORMATION: identity 99

region 1..216

id HUM401H04B

est

# (ix) FEATURE:

- (A) NAME/KEY: other
- (B) LOCATION: 137..303
- (C) IDENTIFICATION METHOD: blastn
- (D) OTHER INFORMATION: identity 95

region 92..258

id T78771

est

#### (ix) FEATURE:

- (A) NAME/KEY: sig\_peptide
- (B) LOCATION: 23..127
- (C) IDENTIFICATION METHOD: Von Heijne matrix
- (D) OTHER INFORMATION: score 7.4

seq SLLLSLELASGSG/QG

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 204:

AAAGGGCGGA STTCAGGTCT CC ATG GAG GCG GCT TCT CCT AGC AAC TCG ACG Net Glu Ala Ala Ser Pro Ser Asn Ser Thr -35														52		
GGC Gly -25	GTT Val	GAG Glu	CGG Arg	ASC Xaa	GCT Ala -20	GAC Asp	CTG Leu	ATG Met	GAC Asp	GCC Ala -15	Asp	AGC Ser	CTC Leu	CTG Leu	CTG Leu -10	100
TCT Ser	CTG Leu	GAG Glu	CTG Leu	GCG Ala -5	TCC Ser	GGC Gly	AGT Ser	GGG Gly	CAG Gln 1	GGC Gly	CTC Leu	AGC Ser	CCG Pro 5	GAC Asp	CGT Arg	148
CGG Arg	GCC Ala	TCG Ser 10	CTG Leu	CTC Leu	ACG Thr	TCT Ser	CTT Leu 15	ATG Met	CTG Leu	GTT Val	AAG Lys	CGC Arg 20	GAC Asp	TAC Tyr	CGC Arg	196
TAT Tyr	GAT Asp 25	CGG Arg	GTT Val	CTC Leu	TTC Phe	TGG Trp 30	GGC Gly	CGC Arg	ATC Ile	CTT Leu	GGC Gly 35	CTC Leu	GTC Val	GCC Ala	GAT Asp	244
TAC Tyr 40	TAC Tyr	ATC Ile	GCG Ala	CAG Gln	GGC Gly 45	CTG Leu	AGT Ser	GAG Glu	GAC Asp	CAG Gln 50	CTC Leu	GCA Ala	CCG Pro	CGC Arg	AAG Lys 55	292
ACG Thr	CTC Leu	TAT Tyr	AGG Arg	TCC Ser 60	AGA Arg	TCA Ser	AGG Arg	AAG Lys	AGA Arg 65	CCC Pro	GCA Ala	CTG Leu				331

# (2) INFORMATION FOR SEQ ID NO: 205:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 317 base pairs
- (B) TYPE: NUCLEIC ACID
- (C) STRANDEDNESS: DOUBLE (D) TOPOLOGY: LINEAR
- (ii) MOLECULE TYPE: CDNA
- (vi) ORIGINAL SOURCE:
  - (A) ORGANISM: Homo Sapiens
  - (F) TISSUE TYPE: Brain
- (ix) FEATURE:
  - (A) NAME/KEY: other
  - (B) LOCATION: 46..119
  - (C) IDENTIFICATION METHOD: blastn
  - (D) OTHER INFORMATION: identity 93 region 12..85 id N80892
- (ix) FEATURE:
  - (A) NAME/KEY: other
  - (B) LOCATION: 38..119
  - (C) IDENTIFICATION METHOD: blastn
  - (D) OTHER INFORMATION: identity 100 region !..32 id #92300

est

1	iх	١	FEATURE:	
١.	ΤX		FEATURE:	

(A) NAME/KEY: sig\_peptide

(B) LOCATION: 108..236

- (C) IDENTIFICATION METHOD: Von Heijne matrix
- (D) OTHER INFORMATION: score 7.4

seq VLVKLLSSSASTS/RP

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 205:

AGTTTCGNST CGCGGATCCG GTAGGTCCAG GTGCAGCGGC CGCAGTKCTG CGTCCGTGCG 60 CCGCGGGCTG GGGCGGTCTC AGGTGTGCCG AAGCTCTGGT CAGTGCC ATG ATC CGG 116 Met Ile Arg CAG GAG CGC TCC ACA TCC TAC CAG GAG GCT GTG CGT CCA GCG CTT CCT Gln Glu Arg Ser Thr Ser Tyr Gln Glu Ala Val Arg Pro Ala Leu Pro -40 -35 TCA AGC AAG CCC TGC CTC CTC ACT TCT CCA GCT GTA TTA GTG AAA CTG 212 Ser Ser Lys Pro Cys Leu Leu Thr Ser Pro Ala Val Leu Val Lys Leu -20 CTC TCC TCC GCC TCC ACT TCT CGG CCC CCA GAC CTT GGT CAT CTT 260 Leu Ser Ser Ser Ala Ser Thr Ser Arg Pro Pro Asp Leu Gly His Leu -5 TGG CAA CCG TCC TCT TCT GTG CCC CTC CAT CGG CCG CCA CAC ACT GCA 308 Trp Gln Pro Ser Ser Ser Val Pro Leu His Arg Pro Pro His Thr Ala 10 15 CCA CCA GCG 317 Pro Pro Ala

### (2) INFORMATION FOR SEQ ID NO: 206:

25

- (i) SEQUENCE CHARACTERISTICS:
  - (A) LENGTH: 363 base pairs
  - (B) TYPE: NUCLEIC ACID
  - (C) STRANDEDNESS: DOUBLE
  - (D) TOPOLOGY: LINEAR
- (ii) MOLECULE TYPE: CDNA
- (vi) ORIGINAL SOURCE:
  - (A) ORGANISM: Homo Sapiens
  - (F) TISSUE TYPE: Brain
- (ix) FEATURE:
  - (A) NAME/KEY: other
  - (B) LOCATION: 26..365
  - (C) IDENTIFICATION METHOD: blastn
  - (D) OTHER INFORMATION: identity 96 region 1..340

id N40260

est

(ix) FEATURE:

(A) NAME/KEY: other
(B) LOCATION: 17..308

(C) IDENTIFICATION METHOD: blastn

(D) OTHER INFORMATION: identity 93

region 6..297 id W07706

est

(ix) FEATURE:

(A) NAME/KEY: other
(B) LOCATION: 311..349

(C) IDENTIFICATION METHOD: blastn

(D) OTHER INFORMATION: identity 100

region 301..339 id W07706

est

(ix) FEATURE:

(A) NAME/KEY: other

(B) LOCATION: 79..365

(C) IDENTIFICATION METHOD: blastn

(D) OTHER INFORMATION: identity 95

region 22..308 id W37568

est.

(ix) FEATURE:

(A) NAME/KEY: other

(B) LOCATION: 140..326

(C) IDENTIFICATION METHOD: blastn

(D) OTHER INFORMATION: identity 93

region 74..260 id W00732

est.

(ix) FEATURE:

(A) NAME/KEY: other

(B) LOCATION: 328..365

(C) IDENTIFICATION METHOD: blastn

(D) OTHER INFORMATION: identity 100

region 263..300

id W00732

est

(ix) FEATURE:

(A) NAME/KEY: other

(B) LOCATION: 79..362

(C) IDENTIFICATION METHOD: blastn

(D) OTHER INFORMATION: identity 95

region 14..297 id AA135041

est

(1K) FEATURE:

(A) NAME/KEY: sig\_peptide

(B) LOCATION: 25..147

(C) IDENTIFICATION METHOD: Von Heijne matrix

(D) OTHER INFORMATION: score 7.4

seq ULPLLFGCLGVFG/LF

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 206:

ACAC	GTCA	CT 1	CCGA	AGGCG	GG G		1et 1				GAC ' Asp '	Tyr (				51
GGC Gly	TAC Tyr	CAG Gln -30	GAA Glu	GAG Glu	TCT Ser	GCC Ala	GAA Glu -25	GTG Val	AAG Lys	GCC Ala	ATG Met	GAC Asp -20	TTC Phe	ATC Ile	ACC Thr	99
TCC Ser	ACA Thr -15	GCC Ala	ATC Ile	CTG Leu	CCC Pro	CTG Leu -10	CTG Leu	TTC Phe	GGC Gly	TGC Cys	CTG Leu -5	GGC Gly	GTC Val	TTC Phe	GGC Gly	147
CTC Leu 1	TTC Phe	CGG Arg	CTG Leu	CTG Leu 5	CAG Gln	TGG Trp	GTG Val	CGC Arg	GGG Gly 10	Lys	GCC Ala	TAC Tyr	CTG Leu	CGG Arg 15	AAT Asn	195
											CTG Leu					243
											GTG Val					291
											CTC Leu 60	Thr				339
			GTG Val							•						363

# (2) INFORMATION FOR SEQ ID NO: 207:

- (i) SEQUENCE CHARACTERISTICS:
  - (A) LENGTH: 235 base pairs
  - (B) TYPE: NUCLEIC ACID
  - (C) STRANDEDNESS: DOUBLE
  - (D) TOPOLOGY: LINEAR
- (ii) MOLECULE TYPE: CDNA
- (vi) ORIGINAL SOURCE:
  - (A) ORGANISM: Homo Sapiens
  - (F) TISSUE TYPE: Brain
- (ix) FEATURE:
  - (A) NAME/KEY: other
  - (B) LOCATION: 60..181
  - (C) IDENTIFICATION METHOD: blastn
  - (D) OTHER INFORMATION: identity 97 region 1..122 id AA057454

est

(1x) FEATURE: (A) NAME/KEY: other (B) LOCATION: 182..233 (C) IDENTIFICATION METHOD: blastn (D) OTHER INFORMATION: identity 96 region 122..173 id AA057454 est (ix) FEATURE: (A) NAME/KEY: other (B) LOCATION: 71..233 (C) IDENTIFICATION METHOD: blastn (D) OTHER INFORMATION: identity 99 region 1..163 id C18312 est (ix) FEATURE: (A) NAME/KEY: other (B) LOCATION: 182..233 (C) IDENTIFICATION METHOD: blastn (D) OTHER INFORMATION: identity 100 region 144..195 id W69247 est (ix) FEATURE: (A) NAME/KEY: other (B) LOCATION: 98..144 (C) IDENTIFICATION METHOD: blastn (D) OTHER INFORMATION: identity 100 region 62..108 id W69247 est (ix) FEATURE: (A) NAME/KEY: other (B) LOCATION: 34..78 (C) IDENTIFICATION METHOD: blastn (D) OTHER INFORMATION: identity 97 region 1..45 id W69247 est (ix) FEATURE: (A) NAME/KEY: other (B) LOCATION: 146..233 (C) IDENTIFICATION METHOD: blastn (D) OTHER INFORMATION: identity 100 region 69..156 id H75891 est (ix) FEATURE: (A) NAME/KEY: other (B) LOCATION: 76..144

> (C) IDENTIFICATION METHOD: blastn (D) OTHER INFORMATION: identity 95

> > region 1..69

est	
(ix) FEATURE:  (A) NAME/KEY: other  (B) LOCATION: 80233  (C) IDENTIFICATION METHOD: blastn  (D) OTHER INFORMATION: identity 98  region 1154  id HUML11265  est	
<pre>(ix) FEATURE:     (A) NAME/KEY: sig_peptide     (B) LOCATION: 104160     (C) IDENTIFICATION METHOD: Von Heijne matrix     (D) OTHER INFORMATION: score 7.4</pre>	
(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 207:	
ATAAGGGGGA ACCCGCTGGC CCAATGGCAG CGTCCTACAG TGTAGCCTCC GCCTCCCGAT	60
TGACTGGCCT GCTTGGCAAK GCAAGTAGCG GCGGCGCTTC AAG ATG CGC TGC CTG Met Arg Cys Leu	115
ACC ACG CCT ATG CTG CTG CGG GCC CTG GCC CAG GCT GCA CGT GCA GGA Thr Thr Pro Met Leu Arg Ala Leu Ala Gln Ala Arg Ala Gly -15 -10 -5 1	163
CCT CCT GGT GGC CGG AGC CTC CAC AGC AGT GCA GTG GCA GCC ACC TAC Pro Pro Gly Gly Arg Ser Leu His Ser Ser Ala Val Ala Ala Thr Tyr 5 10 15	211
AAG TAT GTG AAC ATG CAG GAT CAA Lys Tyr Val Asn Met Gln Asp Gln 20 25	235
(2) INFORMATION FOR SEQ ID NO: 208:  (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 385 base pairs (B) TYPE: NUCLEIC ACID (C) STRANDEDNESS: DOUBLE (D) TOPOLOGY: LINEAR  (ii) MOLECULE TYPE: CDNA  (vi) ORIGINAL SOURCE: (A) ORGANISM: Homo Sapiens (F) TISSUE TYPE: Brain  (ix) FEATURE: (A) NAME/KEY: other (B) LOCATION: 70351 (C) IDENTIFICATION METHOD: blastn (D) OTHER INFORMATION: identity 97 region 34315 id T19063	

est

(ix) FEATURE:

(A) NAME/KEY: other

(B) L∂CATION: 36..68

(C) IDENTIFICATION METHOD: blastn

(D) OTHER INFORMATION: identity 96

region 1..33 id T19063

est

(ix) FEATURE:

(A) NAME/KEY: other

(B) LOCATION: 61..353

(C) IDENTIFICATION METHOD: blastn

(D) OTHER INFORMATION: identity 98

region 1..293 id T32338 est

(ix) FEATURE:

(A) NAME/KEY: other

(B) LOCATION: 93..360

(C) IDENTIFICATION METHOD: blastn

(D) OTHER INFORMATION: identity 99

region 1..268 id T30463

est

(ix) FEATURE:

(A) NAME/KEY: other

(B) LOCATION: complement (107..265)

(C) IDENTIFICATION METHOD: blastn

(D) OTHER INFORMATION: identity 91

region 330..488

id W27204

est

(ix) FEATURE:

(A) NAME/KEY: other

(B) LOCATION: complement (257..385)

(C) IDENTIFICATION METHOD: blastn

(D) OTHER INFORMATION: identity 99

region 209..337

id W27204

est

(ix) FEATURE:

(A) NAME/KEY: other

(B) LOCATION: 70..324

(C) IDENTIFICATION METHOD: blastn

(D) OTHER INFORMATION: identity 99

region 27..281

id T32187

est

(ix) FEATURE:

(A) NAME/KEY: sig\_paptide

(B) LOCATION: 134..331

(C) IDENTIFICATION METHOD: Von Heijne matrix

(D) OTHER INFORMATION: score 7

# seq IWTLLSSVIRCLC/AI

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 208:

AGAC	CAAA	rgg d	CTCAC	GTGC	SA CI	CCGG	GCT	G GAC	CTG	гсст	GGGG	GAGO	CTT (	STTTC	GCGGCA	60
SGGC	CTGCT	rgc 1	rgcc <i>i</i>	ACTGO	T G	GCT	GSGC	cco	CGGTC	CGCC	AGG	AAAA	AAG (	сстс	CCACG	120
TTTC	GAGG	GGA (	STC A		Ser A					/al I				rgg ( rp I		169
			TCC Ser													21,7
GAC Asp	CAC His	ACT Thr	TTT Phe	CTC Leu -35	TAT Tyr	GAA Glu	AAG Lys	CTC Leu	TAC Tyr -30	ACT Thr	GGC Gly	AAG Lys	CCA Pro	AAC Asn -25	CTT Leu	265
			CTC Leu -20													313
			CGC Arg													361
			ACA Thr													385

# (2) INFORMATION FOR SEQ ID NO: 209:

- (i) SEQUENCE CHARACTERISTICS:
  - (A) LENGTH: 285 base pairs
  - (B) TYPE: NUCLEIC ACID
  - (C) STRANDEDNESS: DOUBLE
  - (D) TOPOLOGY: LINEAR
- (ii) MOLECULE TYPE: CDNA
- (vi) ORIGINAL SOURCE:
  - (A) ORGANISM: Homo Sapiens
  - (F) TISSUE TYPE: Brain
- (ix) FEATURE:
  - (A) NAME/KEY: other
  - (B) LOCATION: complement(2..55)
  - (C) IDENTIFICATION METHOD: blastn
  - (D) OTHER INFORMATION: identity 92 region 34..87 id T86932

est

- (ix) FEATURE:
  - (A) NAME/KEY: other
  - (B) LOCATION: complement (45..86)

id T86932 est

(ix) FEATURE:

(A) NAME/KEY: sig\_peptide

(B) LOCATION: 199..240

(C) IDENTIFICATION METHOD: Von Heijne matrix

(D) OTHER INFORMATION: score 6.8

seq IFLTLSLDSRVSA/IR

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 209:

AAATAAAAAT ATCTTAAAAC TGCATTGTAC AGCTCCCTCC CTGCGTTTTA TTAAATGATG 60

TATATTAAAC AAAGATCAAT ATTTTCTTAA TGACTCAGGG TCTTTATTGT TAATGCCAAT 120

TGTTTTTGTA TCTGTGCTAT AATCCCTTAG AGTCAGTAAA GTATGTAGGG GACTGTTTCT 180

TCCTTTGTGT CTGGGTTT ATG ATT TTT CTC ACT CTT TCT TTG GAC TCC AGG 231

Met Ile Phe Leu Thr Leu Ser Leu Asp Ser Arg -10

GTG TCA GCC ATC AGG TCT CCT AAT TTT GTG TAC CGG TCT CCA ACA DMC 279

Val Ser Ala 1le Arg Ser Pro Asn Phe Val Tyr Arg Ser Pro Thr Xaa 1 5 10

CAT GGG
His Gly

(2) INFORMATION FOR SEQ ID NO: 210:

15

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 378 base pairs

(B) TYPE: NUCLEIC ACID

(C) STRANDEDNESS: DOUBLE

(D) TOPOLOGY: LINEAR

(ii) MOLECULE TYPE: CDNA

(vi) ORIGINAL SOURCE:

(A) ORGANISM: Homo Sapiens

(F) TISSUE TYPE: Brain

(ix) FEATURE:

(A) NAME/KEY: other

(B) LOCATION: 65..270

(0) IDENTIFICATION METHOD: blastn

(D) OTHER INFORMATION: identity 97 region 109..314 id AA100852 est

(ix) ESATURE:

(3) NAME/KEY: other

(B) LOCATION: 269..378

(C) IDENTIFICATION METHOD: blastn

(D) OTHER INFORMATION: identity 94

region 314..423

id AA100852

est

### (ix) FEATURE:

- (A) NAME/KEY: other
- (B) LOCATION: 65..270
- (C) IDENTIFICATION METHOD: blastn
- (D) OTHER INFORMATION: identity 97

region 109..314

id AA161042

est

### (ix) FEATURE:

- (A) NAME/KEY: other
- (B) LOCATION: 277..361
- (C) IDENTIFICATION METHOD: blastn
- (D) OTHER INFORMATION: identity 94

region 323..407

id AA161042

est

### (ix) FEATURE:

- (A) NAME/KEY: other
- (B) LOCATION: 65..274
- (C) IDENTIFICATION METHOD: blastn
- (D) OTHER INFORMATION: identity 97

region 104..313

id H64488

est

# (ix) FEATURE:

- (A) NAME/KEY: other
  - (B) LOCATION: 68..256
  - (C) IDENTIFICATION METHOD: blastn
  - (D) OTHER INFORMATION: identity 97

region 147..335 id AA146605

est

### (ix) FEATURE:

- (A) NAME/KEY: other
- (B) LOCATION: 256..317
- (C) IDENTIFICATION METHOD: blastn
- (D) OTHER INFORMATION: identity 96

region 336..397

id AA146605

est

#### (ix) FEATURE:

- (A) NAME/KEY: other
- (B) LOCATION: 80..305
- (C) IDENTIFICATION METHOD: blastn
- (D) OTHER INFORMATION: identity 98

region 129..354

id AA088770 est WO 99/06552 PCT/IB98/01236

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CTC	TTC	AAT	TTG	CTC	ATC	TTT	CTG	TGT	GGT	GCA	GCC	CTG	TTR	RCA	GTG	159
Leu	Phe	Asn	Leu	Leu	Ile	Phe	Leu	Cys	Gly	Ala	Ala	Leu	Leu	Xaa	Val	
		-15					-10					<b>-</b> 5				
						GAT										207
Gly		Trp	Val	Ser	Ile	Asp	Gly	Ala	Ser	Phe	Leu	Lys	Ile	Phe	Gly	
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Pro	Leu	Ser	Ser		Ala	Met	GIn	Phe		Asn	Val	Gly	Tyr		Leu	
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						GTC Val										303
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			22					40					43			
SGT	GCT	AAG	ACT	GAG	AGC	WAG	TGT	GCC	СТС	GTG	ACG	TTC	TTC	TKC	ΔTC	351
						Xaa										331
		50					55					60				
CTC	CTS	CTC	ATC	TTC	ATT	GCT	GAC	GTT								378
Leu	Leu	Leu	Ile	Phe	Ile	Ala	Asp	Val								
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(2)	INE	ORMA	TION	FOR	SEQ	ID	NO:	211:								
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	(	ii)	MOLE	CULF.	TYP	E: C	DNA									
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						TYPE										

(12 FEATURE:

(A) NAME/KEY: other
(B) LOCATION: 234..283
(C) IDENTIFICATION METHOD: blastn

(D) OTHER INFORMATION: identity 96

region 203..257

id R25833 est

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(A) NAME/KEY: other
(B) LOCATION: 285..317

(C) IDENTIFICATION METHOD: blastn

(D) OTHER INFORMATION: identity 100 region 255..287 id R25833

est

# (ix) FEATURE:

(A) NAME/KEY: sig\_peptide

(B) LOCATION: 37..141

(C) IDENTIFICATION METHOD: Von Heijne matrix

(D) OTHER INFORMATION: score 6.4

seq SACLLLCPTWTNP/QL

# (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 211:

AAAA	AAGG	CG G	GGTC	TCGG	SC CG	GCGC	TGAC	GC#	(GCC		GCG Ala		54
	GCC Ala												102
_	GCG Ala												150
	ACT Thr 5												198
	ACG Thr												246
	TTC Phe												294
	GAT Asp												327

# (2) INFORMATION FOR SEQ ID NO: 212:

# (i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 244 base pairs

(B) TYPE: NUCLEIC ACID

(C) STRANDEDNESS: DOUBLE

(D) TOPOLOGY: LINEAR

199 (i1) MOLECULE TYPE: CDNA (vi) ORIGINAL SOURCE: (A) ORGANISM: Homo Sapiens (F) TISSUE TYPE: Brain (ix) FEATURE: (A) NAME/KEY: other (B) LOCATION: 82..241 (C) IDENTIFICATION METHOD: blastn (D) OTHER INFORMATION: identity 99 region 51..210 id C18780 est (ix) FEATURE: (A) NAME/KEY: other (B) LOCATION: 48..83 (C) IDENTIFICATION METHOD: blastn (D) OTHER INFORMATION: identity 94 region 18..53 id C18780 est (ix) FEATURE: (A) NAME/KEY: other (B) LOCATION: 163..235 (C) IDENTIFICATION METHOD: blastn (D) OTHER INFORMATION: identity 97 region 121..193 id T11911 est (ix) FEATURE: (A) NAME/KEY: other (B) LOCATION: 116..162 (C) IDENTIFICATION METHOD: blastn (D) OTHER INFORMATION: identity 95 region 73..119 id T11911 est (ix) FEATURE: (A) NAME/KEY: other (B) LOCATION: 204..239 (C) IDENTIFICATION METHOD: blastn (D) OTHER INFORMATION: identity 94 region 226..261 id T69629 (ix) FEATURE: (A) NAME/KEY: sig\_peptide (B) LOCATION: 143..199 (C) IDENTIFICATION METHOD: Von Heijne matrix (D) OTHER INFORMATION: score 6.4 seq SVFLLMVNGQVES/AQ

(HL) SEQUENCE DESCRIPTION: SEQ ID NO: 212:

AGCACTCGCG TGGCCTTCGC GAAGGTGTCG CTGCCAAGAA ACGTGTCCTG CGCGCTACGC 60 CGTCTGTTTT TAGGGCAACG CCGGCGTCTC TTAGCAACCG CGCGCGCCT AGGTGGGTCC 120 CCCCGGCACC CCCAGACCTG CC ATG GCG ACC GCG AGT CCT AGC GTC TTT CTA Met Ala Thr Ala Ser Pro Ser Val Phe Leu -15 CTC ATG GTC AAC GGG CAG GTG GAG AGC GCC CAG TTT CCA GAG TAT GAT 220 Leu Met Val Asn Gly Gln Val Glu Ser Ala Gln Phe Pro Glu Tyr Asp 1 GAC CTC TAC TGC AAG TAC TGC CAG 244 Asp Leu Tyr Cys Lys Tyr Cys Gln 10 15

# (2) INFORMATION FOR SEQ ID NO: 213:

- (i) SEQUENCE CHARACTERISTICS:
  - (A) LENGTH: 211 base pairs
  - (B) TYPE: NUCLEIC ACID
  - (C) STRANDEDNESS: DOUBLE
  - (D) TOPOLOGY: LINEAR
- (ii) MOLECULE TYPE: CDNA
- (vi) ORIGINAL SOURCE:
  - (A) ORGANISM: Homo Sapiens
  - (F) TISSUE TYPE: Brain
- (ix) FEATURE:
  - (A) NAME/KEY: other
  - (B) LOCATION: 95..208
  - (C) IDENTIFICATION METHOD: blastn
  - (D) OTHER INFORMATION: identity 100 region 85..198 id N43024 est

- (ix) FEATURE:
  - (A) NAME/KEY: other
  - (B) LOCATION: 28..95
  - (C) IDENTIFICATION METHOD: blastn
  - (D) OTHER INFORMATION: identity 91 region 17..84 id N43024

est

est

- (ix) FEATURE:
  - (A) NAME/KEY: other
  - (B) LOCATION: 107..199
  - (C) IDENTIFICATION METHOD: blastn
  - (D) OTHER INFORMATION: identity 98 region 80..172 id T62095

(ix) FEATURE: (A) NAME/KEY: other

201 (B) LOCATION 61..106 (C) IDENTIFE WITTON METHOD: blastn (D) OTHER PROGRATION: identity 93 region 35..80 id T62095 est (ix) FEATURE: (A) NAME/KEY: other (B) LOCATION: 26..60 (C) IDENTIFICATION METHOD: blastn (D) OTHER INFORMATION: identity 97 region 1..35 id T62095 est (ix) FEATURE: (A) NAME/KEY: other (B) LOCATION: 61..208 (C) IDENTIFICATION METHOD: blastn (D) OTHER INFORMATION: identity 98 region 26..173 id W42796 est (ix) FEATURE: (A) NAME/KEY: other (B) LOCATION: 110..208 (C) IDENTIFICATION METHOD: blastn (D) OTHER INFORMATION: identity 92 region 114..212 id AA030227 est (ix) FEATURE: (A) NAME/REY: other (B) LOCATION: 110..208 (C) IDENTIFICATION METHOD: blastn (D) OTHER INFORMATION: identity 92 region 51..149 id AA118270 est (ix) FEATURE: (A) NAME/KEY: sig\_peptide (B) LOCATION: 104..187 (C) IDENTIFICATION METHOD: Von Heijne matrix (D) OTHER INFORMATION: score 6 seq IGLMFLMLGCALP/IY (M1) SEQUENCE DESCRIPTION: SEQ ID NO: 213: TOTTCCGGGT GTTGTCTGGA CGCCGTAGCG CRTCTTGGGT CTCCCGGCTG CCGCTGCTGC 60 CGCCGCCGCC TCGGGTCGT3 CAGCCAGGAG CGACGTCACC GCC ATG GCA GGC ATC 115 Met Ala Gly Ile

AMA GOT TTG ATT AGT TITE VEC TIT GGA GGA GCA ATC GGA CTG ATG TIT Lys Ala Leu Ile Ser her Her She Gly Gly Ala Ile Gly Leu Met Phe

-25

WO 99/06552 PCT/IB98/01236

-20 -15 -10

TTG ATG CTT GGA TGT GCC CTT CCA ATA TAC AAC AAA TAC TGG CCC TGG
Leu Met Leu Gly Cys Ala Leu Pro Ile Tyr Asn Lys Tyr Trp Pro Trp

-5

1

5

# (2) INFORMATION FOR SEQ ID NO: 214:

- (i) SEQUENCE CHARACTERISTICS:
  - (A) LENGTH: 128 base pairs
  - (B) TYPE: NUCLEIC ACID
  - (C) STRANDEDNESS: DOUBLE
  - (D) TOPOLOGY: LINEAR
- (ii) MOLECULE TYPE: CDNA
- (vi) ORIGINAL SOURCE:
  - (A) ORGANISM: Homo Sapiens
  - (F) TISSUE TYPE: Brain
- (ix) FEATURE:
  - (A) NAME/KEY: other
  - (B) LOCATION: 3..124
  - (C) IDENTIFICATION METHOD: blastn
  - (D) OTHER INFORMATION: identity 99

region 8..129 id AA146587

est

- (ix) FEATURE:
  - (A) NAME/KEY: other
  - (B) LOCATION: 2..124
  - (C) IDENTIFICATION METHOD: blastn
  - (D) OTHER INFORMATION: identity 98

region 14..136

id T85006

est

- (ix) FEATURE:
  - (A) NAME/KEY: other
  - (B) LOCATION: 11..124
  - (C) IDENTIFICATION METHOD: blastn
  - (D) OTHER INFORMATION: identity 100

region 1..114

id H08511

est

- (ix) FEATURE:
  - (A) NAME/KEY: other
  - (B) LOCATION: 14..124
  - (C) IDENTIFICATION METHOD: blastn
  - (D) OTHER INFORMATION: identity 98

region 1..111

id C00740

est

- (ix) FEATURE:
  - (A) NAME/KEY: other
  - (B) LOCATION: 13..124

50

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128

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	(C) IDENTI (D) OTHER	FICATION ME INFORMATION	l: identi	ty 98 1112	1017
		N: 1262 ICATION ME NFORMATION	THOD: Von : score : seq ILI	FGTLLMNAGA/VL	
(xi)	SEQUENCE DES	CRIPTION:	SEQ ID NO:	214:	
	-1	5	ocu Leu Pr -1		Leu Met -5
AAT GCC GGG Asn Ala Gly	GCG GTG CTG Ala Val Leu l	AAC TTT AAAASn Phe Ly	AG CTG AAA vs Leu Lys 5	AAG AAG GAC . Lys Lys Asp	ACG CAG Thr Gln
GGC TTT GGG Gly Phe Gly 15	GAG GAG TCC Glu Glu Ser	AGG GAG CO Arg Glu Pr 20	T TGG O Trp		1
(2) INFORMAT	ION FOR SEQ	ID NO: 215	:		
(i) SE	QUENCE CHARA (A) LENGTH: (B) TYPE: NU (C) STRANDED (D) TOPOLOGY	CTERISTICS 150 base po CLEIC ACID NESS: DOUB!	: Birs		
(ii) M	OLECULE TYPE	: CDNA			
	RIGINAL SOUR (A) ORGANISM (F) TISSUE TY	: Homo Sani	ėns		
. (	CATURE:  A) NAME/KEY: B) LOCATION: C) IDENTIFIC D) OTHER INE	12143 CATION METH	OD: blast identity region 3 id HUM13 est	99 6167	
(	ATURE: A) NAME/KEY: B) LOCATION: C) IDENTIFIC D) OTHER INF	12142 ATION METH	DD: blastr identity region 14 id AA1559 est	99  3273	

- (ix) FEATURE: (A) NAME/KEY: other
  - (B) LOCATION: 12..141
  - (C) IDENTIFICATION METHOD: blastn
  - (D) OTHER INFORMATION: identity 99

region 115..244

id W39572

est

### (ix) FEATURE:

- (A) NAME/KEY: other
- (B) LOCATION: complement (12..135)
- (C) IDENTIFICATION METHOD: blastn
- (D) OTHER INFORMATION: identity 95

region 1..124 id M78698

est

### (ix) FEATURE:

- (A) NAME/KEY: other
- (B) LOCATION: complement (32..151)
- (C) IDENTIFICATION METHOD: blastn
- (D) OTHER INFORMATION: identity 98

region 346..465

id H99266

#### (ix) FEATURE:

- (A) NAME/KEY: sig\_peptide
- (B) LOCATION: 67..114
- (C) IDENTIFICATION METHOD: Von Heijne matrix
- (D) OTHER INFORMATION: score 5.9

seq MILTLSLFGSCIS/NF

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 215:

ACACATCCCT CTAAACTACT GTTAGGAACA GCAGTGTTCT CACAGTGTRG GGCAGCCGTC

CTTCTA ATG AAG ACA ATG ATA TTG ACA CTG TCC CTC TTT GGC AGT TGC Met Lys Thr Met Ile Leu Thr Leu Ser Leu Phe Gly Ser Cys -15 -10

ATT AGT AAC TIT GAA AGG TAT ATG ACT GAG CGT AGC ATC CAG 150 Ile Ser Asn Phe Glu Arg Tyr Met Thr Glu Arg Ser Ile Gln

# (2) INFORMATION FOR SEQ ID NO: 216:

- (i) SEQUENCE CHARACTERISTICS:
  - (A) LENGTH: 397 base pairs
  - (B) TYPE: NUCLEIC ACID
  - (C) STRANDEDNESS: DOUBLE
  - (D) TOPOLOGY: LINEAR
- (ii) MOLECULE TYPE: CDNA
- (vi) ORIGINAL SOURCE:

WO 99/06552 PCT/IB98/01236

205 (A) OKCANISM: Homo Sapiens (F) TISSUE TYPE: Brain (ix) FEATURE: (A) NAME/KEY: other (B) LOCATION: complement(223..398) (C) IDENTIFICATION METHOD: blastn (D) OTHER INFORMATION: identity 96 region 111..286 id HSGT545 est (ix) FEATURE: (A) NAME/KEY: other (B) LOCATION: complement(69..219) (C) IDENTIFICATION METHOD: blastn (D) OTHER INFORMATION: identity 92 region 291..441 id HSGT545 est (ix) FEATURE: (A) NAME/KEY: other (B) LOCATION: complement(2..43) (C) IDENTIFICATION METHOD: blastn (D) OTHER INFORMATION: identity 97 region 467..508 id HSGT545 est (ix) FEATURE: (A) NAME/KEY: other (B) LOCATION: complement (223..311) (C) IDENTIFICATION METHOD: blastn (D) OTHER INFORMATION: identity 92 region 4..92 id AA036134 est (ix) FEATURE: (A) NAME/KEY: other (B) LOCATION: complement (46..163) (C) IDENTIFICATION METHOD: blastn (D) OTHER INFORMATION: identity 91 region 133..250 id AA038839 est (ix) FEATURE: (A) MAME/KEY: other (B; LOCATION: complement(223..295) (C) IDENTIFICATION METHOD: blastn (D) OTHER INFORMATION: identity 97 region 1..73 id AA038839 est

(ix) FEATURE:

(A, NAME/KEY: other (B) LOCATION: 326..387

(C) IDENTIFICATION METHOD: blastn

(D) OTHER INFORMATION: identity 91 region 2..63 id W51392

est

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(A) NAME/KEY: sig\_peptide

(B) LOCATION: 152..268

(C) IDENTIFICATION METHOD: Von Heijne matrix

(D) OTHER INFORMATION: score 5.9

seq SVSVLSSLGIVLA/VV

(xi) SEQUENCE DESCRIPTION: SEO ID NO: 216:

ACTTTGAGGG TGTCTCTGGC CATGTGGTGT TTGATGCCAG CBGCTCTCGG ATGGCATGGA CGCTTATCGA GCAGCTTCAG GGTGGCAGCT ACAAGAAGAT TGGCTACTAT GACAGCACCA 120 AGGATGATCT TTCCTGGTCC AAAACAGATA A ATG GAT TGG AGG GTC CCC CCC 172 Met Asp Trp Arg Val Pro Pro -35 AGC TGR SCA GAC CCT GGT CAT CAA GAC ATT CCG CTT CCT GTC ACA GAN 220 Ser Xaa Xaa Asp Pro Gly His Gln Asp Ile Pro Leu Pro Val Thr Xaa -30 -25 NNC TTT ATC TCC GTC TCA GTT CTC TCC AGC CTG GGC ATT GTC CTA GCT 268 Xaa Phe Ile Ser Val Ser Val Leu Ser Ser Leu Gly Ile Val Leu Ala -15 -10 GTT GTC TGT CTG TCC TTT AAC ATC TAC AAC TCA CAT GTC CGT TAT ATC 316 Val Val Cys Leu Ser Phe Asn Ile Tyr Asn Ser His Val Arg Tyr Ile 10 CAG AAC TCA CAG CCC AAC CTG AAC CTG ACT GCT GTG GGC TGC TCA 364 Gln Asn Ser Gln Pro Asn Leu Asn Asn Leu Thr Ala Val Gly Cys Ser 20 MTG GCT TTA GCT GCT GTC TTC CCC TGG GGC TCG 397 Xaa Ala Leu Ala Ala Val Phe Pro Trp Gly Ser

# (2) INFORMATION FOR SEQ ID NO: 217:

35

- (i) SEQUENCE CHARACTERISTICS:
  - (A) LENGTH: 373 base pairs

40

- (B) TYPE: NUCLEIC ACID
- (C) STRANDEDNESS: DOUBLE
- (D) TOPOLOGY: LINEAR
- (ii) MOLECULE TYPE: CDNA
- (vi) ORIGINAL SOURCE:
  - (A) ORGANISM: Homo Sapiens
  - (F) TISSUE TYPE: Brain
- (ix) FEATURE:
  - (A) MAME/KEY: other

(B) LOCATION: 41..337 (C) IDENTIFICATION METHOD: blastn (D) OTHER INFORMATION: identity 97 region 1..297 id H56523 (ix) FEATURE: (A) NAME/KEY: other (B) LOCATION: 38..337 (C) IDENTIFICATION METHOD: blastn (D) OTHER INFORMATION: identity 96 region 1..300 id AA020823 (ix) FEATURE: (A) NAME/KEY: other (B) LOCATION: 43..337 (C) IDENTIFICATION METHOD: blastn (D) OTHER INFORMATION: identity 96 region 7..301 id H99096 est (ix) FEATURE: (A) NAME/KEY: other (B) LOCATION: 49..315 (C) IDENTIFICATION METHOD: blastn (D) OTHER INFORMATION: identity 98 region 11..277 id AA083141 est (ix) FEATURE: (A) NAME/KEY: other (B) LOCATION: 52..337 (C) IDENTIFICATION METHOD: blastn (D) OTHER INFORMATION: identity 96 region 17..302 id N21197 (ix) FEATURE: (A) NAME/KEY: sig\_peptide (B) LOCATION: 35..82 (C) IDENTIFICATION METHOD: Von Heijne matrix (D) OTHER INFORMATION: score 5.8 seq AALPAWLSLQSRA/RT (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 217: AGCTTGTCCC CTCCGGCTTG CCGTCCTCGC AGCC ATG GCG GCC GCG CTC CCA Met Ala Ala Ala Leu Pro GCA TGG CTG TUT CTG CAG TCG AGG GCA AGG ACT CTG CGT GCA TTC TCC Ala Trp Leu Ser Leu Gin Ser Arg Ala Arg Thr Leu Arg Ala Phe Ser 1

		TCG Ser							151
		AAT Asn							199
		ATG Met							247
		TTT Phe 60							295
		AAA Lys							343
	qzA	TCC Ser	Asn					,	373

# (2) INFORMATION FOR SEQ ID NO: 218:

- (i) SEQUENCE CHARACTERISTICS:
  - (A) LENGTH: 333 base pairs
  - (3) TYPE: NUCLEIC ACID
  - (C) STRANDEDNESS: DOUBLE
  - (D) TOPOLOGY: LINEAR
- (ii) MOLECULE TYPE: CDNA
- (vi) ORIGINAL SOURCE:
  - (A) ORGANISM: Homo Sapiens
  - (F) TISSUE TYPE: Brain
- (ix) FEATURE:
  - (A) NAME/KEY: other
  - (B) LOCATION: 32..331
  - (C) IDENTIFICATION METHOD: blastn
  - (D) OTHER INFORMATION: identity 99 region 1..300

id R13004

id R130

(ix) FEATURE:

- (A) NAME/KEY: other
- (B) LOCATION: 114..274
- (C) IDENTIFICATION METHOD: blastn
- (D) OTHER INFORMATION: identity 99

region 54..214 id T80337

est

(ix) FEATURE:

(A) NAME/KEY: other

(B) LOCATION: 272..331

(C) IDENTIFICATION METHOD: blastn
(D) OTHER INFORMATION: identity 100
region 213..272
id T80337

est

# (ix) FEATURE:

- (A) NAME/KEY: other
- (B) LOCATION: 66..106
- (C) IDENTIFICATION METHOD: blastn
- (D) OTHER INFORMATION: identity 100

region 6..46 id T80337 est

#### (ix) FEATURE:

- (A) NAME/KEY: other
- (B) LOCATION: 101..278
- (C) IDENTIFICATION METHOD: blastn
- (D) OTHER INFORMATION: identity 94

region 70..247 id T08840 est

### (ix) FEATURE:

- (A) NAME/KEY: other
- (B) LOCATION: 33..113
- (C) IDENTIFICATION METHOD: blastn
- (D) OTHER INFORMATION: identity 98 region 1..81 id T08840 est

### (ix) FEATURE:

- (원) NAME/KEY: other
- (B) LOCATION: 101..249
- (C) IDENTIFICATION METHOD: blastn
- (D) OTHER INFORMATION: identity 95

region 72..220 id HSCOCF041

est

### (ix) FEATURE:

- (A) NAME/KEY: other
- (B) LOCATION: 31..112
- (C) IDENTIFICATION METHOD: blastn
- (D) OTHER INFORMATION: identity 100 region 1..82

region 1..82 id HSCOCF041

est

# (ix) FEATURE:

- (A) NAME/KEY: sig\_peptide
- (B) LOCATION: 247..321
- (C) IDENTIFICATION METHOD: Von Heijne matrix
- (D) OTHER INFORMATION: score 5.8

seq LWISACAMLLCHG/SL

(xi) Figurate description: SEQ ID NO: 218:

AAGCTAGGAC ATTCTTCTCC TCCTGGCCCT GGACATCAGA ACCCCAGGCT CTCCAGCCTT 60

TGGACTTCAG GACTGACACA AGCAACCTGC TGGGTTCTTA GGCCTTTGGC TTGTACTGAG 120

ACTTACACCA TCAGCTTCCC TGGTCCTGAG ACTTTTGGAC TTGGATTGAG CCACGCTACT 180

GGCATCCCAG GATCTCCAGC TTGCAGACAG CCTGTCGTGG GACTTCACAG CCTCCATAAT 240

TATAGA ATG GCA ATG GTC TCT GCG ATG TCC TGG GTC CTG TAT TTG TGG 288

Met Ala Met Val Ser Ala Met Ser Trp Val Leu Tyr Leu Trp -25 -20 -15

ATA AGT GCT TGT GCA ATG CTA CTC TGC CAT GGA TCC CTT CAG CGG 333

Ile Ser Ala Cys Ala Met Leu Leu Cys His Gly Ser Leu Gln Arg -10 -5

# (2) INFORMATION FOR SEQ ID NO: 219:

- (i) SEQUENCE CHARACTERISTICS:
  - (A) LENGTH: 284 base pairs
  - (B) TYPE: NUCLEIC ACID
  - (C) STRANDEDNESS: DOUBLE
  - (D) TOPOLOGY: LINEAR
- (ii) MOLECULE TYPE: CDNA
- (vi) ORIGINAL SOURCE:
  - (A) ORGANISM: Homo Sapiens
  - (F) TISSUE TYPE: Brain
- (ix) FEATURE:
  - (A) NAME/KEY: other
  - (B) LOCATION: complement(2..282)
  - (C) IDENTIFICATION METHOD: blastn
  - (D) OTHER INFORMATION: identity 100 region 59..339 id H10776

est

- (ix) FEATURE:
  - (A) NAME/KEY: other
  - (B) LOCATION: complement(64..282)
  - (C) IDENTIFICATION METHOD: blastn
  - (D) OTHER INFORMATION: identity 96 region 73..291 id N94455

est

- (ix) FEATURE:
  - (A) NAME/KEY: other
  - (B) LOCATION: complement(2..85)
  - (C) IDENTIFICATION METHOD: blastn
  - (D) OTHER INFORMATION: identity 95

region 271..354 id N94455

LU N944.

- (ix) FEATURE:
  - (A) NAME/KEY: other

WO 99/06552 PCT/IB98/01236

211	
(B) LOCATION: domplement(107282) (C) IDENTIFICATION METHOD: blastn (D) OTHER INFORMATION: identity 99 region 58233 id H64097 est	
(ix) FEATURE:  (A) NAME/KEY: other  (B) LOCATION: complement(2120)  (C) IDENTIFICATION METHOD: blastn  (D) OTHER INFORMATION: identity 94  region 219337  id H64097  est	
<pre>(ix) FEATURE:     (A) NAME/KEY: other     (B) LOCATION: complement(38282)     (C) IDENTIFICATION METHOD: blastn     (D) OTHER INFORMATION: identity 99</pre>	
(ix) FEATURE:  (A) NAME/KEY: other  (B) LOCATION: complement(161282)  (C) IDENTIFICATION METHOD: blastn  (D) OTHER INFORMATION: identity 96  region 33154  id W60134  est	
(ix) FEATURE:  (A) NAME/KEY: other  (B) LOCATION: complement(9120)  (C) IDENTIFICATION METHOD: blastn  (D) OTHER INFORMATION: identity 96  region 195306  id W60134  est	
<pre>(ix) FEATURE:    (A) NAME/KEY: sig_peptide    (B) LOCATION: 51257    (C) IDENTIFICATION METHOD: Von Heijne matrix    (D) OTHER INFORMATION: score 5.7</pre>	
(xt) SEQUENCE DESCRIPTION: SEQ ID NO: 219:	
ATCAACCATO CAGCTCCCAG CTGGCTAAAC TTTGCCTCCA GTGGTCAAAG ATG GGA Met Gly	56
AAA GAG TGG GGT TGG CAG GAG ATG GAA AAC GGA GGT GCC GCC CCA GCA Lys Glu Trp Gly Trp Gln Glu Met Glu Asn Gly Gly Ala Ala Pro Ala -60 -55	0 4
TGG GGG CON GGT CCC CCA GTG CAC CCT GCC CCT GCC CCT GTG GAG AAG 1	52

Trp Gly Ala Gly Pro Pro Val His Pro Ala Pro Pro Pro Val Glu Lys
-50 -45 -40

ACG CTT AGT TGG GGG TGT GGG TTT GGG CTC CAT TCT GGA TTC GGC GGT
Thr Leu Ser Trp Gly Cys Gly Phe Gly Leu His Ser Gly Phe Gly Gly

Thr Leu Ser Trp Gly Cys Gly Phe Gly Leu His Ser Gly Phe Gly Gly
-35 -20 -25

TCC GGG GGA GGG GTG GGT CTG TGC CGA TTA CTC TGT CTT GTA CGT TTG

Ser Gly Gly Val Gly Leu Cys Arg Leu Leu Cys Leu Val Arg Leu

-15 -10 -5

TTC TGC TGC TCT TCA ATA TTG TAT CAA CGC CAG GGG
Phe Cys Cys Ser Ser Ile Leu Tyr Gln Arg Gln Gly

1 5

# (2) INFORMATION FOR SEQ ID NO: 220:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 361 base pairs

(B) TYPE: NUCLEIC ACID

(C) STRANDEDNESS: DOUBLE

(D) TOPOLOGY: LINEAR

# (ii) MOLECULE TYPE: CDNA

(vi) ORIGINAL SOURCE:

(A) ORGANISM: Homo Sapiens

(F) TISSUE TYPE: Brain

### (ix) FEATURE:

(A) NAME/KEY: other

(B) LOCATION: 137..358

(C) IDENTIFICATION METHOD: blastn

(D) OTHER INFORMATION: identity 97

region 151..372

id N33828

est

### (ix) FEATURE:

(A) NAME/KEY: other

(B) LOCATION: 2..124

(C) IDENTIFICATION METHOD: blastn

(D) OTHER INFORMATION: identity 99

region 14..136

id N33828

est

# (ix) FEATURE:

(A) NAME/KEY: other

(B) LOCATION: 138..358

(C) IDENTIFICATION METHOD: blastn

(D) OTHER INFORMATION: identity 98

region 147..367

id N34173

est

# (ix) FEATURE:

(A) NAME/KEY: other

(3) LOCATION: 1..148

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213 (C) IDENTIFICATION METHOD: blastn (D) OTHER INFORMATION: identity 98 region 11..158 id N34173 est (ix) FEATURE: (A) NAME/KEY: other (B) LOCATION: 35..358 (C) IDENTIFICATION METHOD: blastn (D) OTHER INFORMATION: identity 99 region 1..324 id T89546 est (ix) FEATURE: (A) NAME/KEY: other (B) LOCATION: 138..337 (C) IDENTIFICATION METHOD: blastn (D) OTHER INFORMATION: identity 98 region 107..306 id H67305 est (ix) FEATURE: (A) NAME/KEY: other (B) LOCATION: 42..148 (C) IDENTIFICATION METHOD: blastn (D) OTHER INFORMATION: identity 99 region 12..118 id H67305 est (ix) FEATURE: (A) NAME/KEY: other (B) LOCATION: 138..302 (C) IDENTIFICATION METHOD: blastn (D) OTHER INFORMATION: identity 98 region 112..276 id T79378 est (ix) FEATURE: (A) NAME/KEY: other (B) LOCATION: 33..145 (C) IDENTIFICATION METHOD: blastn (D) OTHER INFORMATION: identity 100 region 8..120 id T79378 est (ix) FEATURE: (A) NAME/KEY: other (B) LOCATION: 317..348 (C) IDENTIFICATION METHOD: blastn (D) OTHER INFORMATION: identity 100 region 293..324 id T79378

est

214

(A) NAME/KEY: sig\_peptide
(B) LOCATION: 167..229

(C) IDENTIFICATION METHOD: Von Heijne matrix

(D) OTHER INFORMATION: score 5.6

seq LVLSLQFLLLSYD/LF

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 220:

AATGACAACC GACGTTGGAG TTTGGAGGTG CTTGCCTTAG AGCAAGGGAA ACAGCTCTCA 60 TTCAAAGGAA CTAGAAGCCT CTCCCTCAGT GGTAGGGAGA CAGCCAGGAG CGGTTTTCTG 120 GGAACTGTGG GATGTGCCCT TGGGGGCCCG AGAAAACAGA AGGAAG ATG CTC CAG 175 Met Leu Gln -20 ACC AGT AAC TAC AGC CTG GTG CTC TCT CTG CAG TTC CTG CTG CTG TCC 223 Thr Ser Asn Tyr Ser Leu Val Leu Ser Leu Gln Phe Leu Leu Ser -15 TAT GAC CTC TTT GTC AAT TCC TTC TCA GAA CTG CTC CAA AAG ACT CCT 271 Tyr Asp Leu Phe Val Asn Ser Phe Ser Glu Leu Leu Gln Lys Thr Pro 1 5 GTC ATC CAG CTT GTG CTC TTC ATC ATC CAG GAT ATT GCA GTC CTC TTC 319 Val Ile Gln Leu Val Leu Phe Ile Ile Gln Asp Ile Ala Val Leu Phe 15 20 25 AAC ATC ATC ATT TTC CTC ATG TTC TTC AAC ACC TCC CGG 361 Asn Ile Ile Ile Phe Leu Met Phe Phe Asn Thr Ser Arg

### (2) INFORMATION FOR SEQ ID NO: 221:

- (i) SEQUENCE CHARACTERISTICS:
  - (A) LENGTH: 252 base pairs
  - (B) TYPE: NUCLEIC ACID
  - (C) STRANDEDNESS: DOUBLE
  - (D) TOPOLOGY: LINEAR
- (ii) MOLECULE TYPE: CDNA
- (vi) ORIGINAL SOURCE:
  - (A) ORGANISM: Homo Sapiens
  - (F) TISSUE TYPE: Brain
- (ix) FEATURE:
  - (A) NAME/KEY: other
  - (B) LOCATION: complement(100..250)
  - (C) IDENTIFICATION METHOD: blastn
  - (D) OTHER INFORMATION: identity 95

region 256..406

id W72958

est

- (iz) FEATURE:
  - (A) NAME/KEY: other
  - (B) LOCATION: 115..250

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(IX) FEATURE: (A) NAME/KEY: other (B) LOCATION: 120250 (C) IDENTIFICATION METHOD: blastn (D) OTHER INFORMATION: identity 99		(C) IDENTIFICATION METHO (D) OTHER INFORMATION:		
(A) NAME/KEY: other (B) LOCATION: 115250 (C) IDENTIFICATION METHOD: blastn (D) OTHER INFORMATION: identity 98	(ix)	(A) NAME/KEY: other (B) LOCATION: 120250 (C) IDENTIFICATION METHO	identity 99 region 1131 id AA083784	
(A) NAME/KEY: other (B) LOCATION: 145250 (C) IDENTIFICATION METHOD: blastn (D) OTHER INFORMATION: identity 97	(ix)	(A) NAME/KEY: other (B) LOCATION: 115250 (C) IDENTIFICATION METHO	identity 98 region 4139 id W24219	
(A) NAME/KEY: other (B) LOCATION: 114153 (C) IDENTIFICATION METHOD: blastn (D) OTHER INFORMATION: identity 95	(ix)	(A) NAME/KEY: other (B) LOCATION: 145250 (C) IDENTIFICATION METHO	identity 97 region 39144 id C15963	
(A) NAME/KEY: sig_peptide (B) LOCATION: 172243 (C) IDENTIFICATION METHOD: Von Heijne matrix (D) OTHER INFORMATION: score 5.5 seq MGVCLLIPGLATA/CI  (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 221:  30300GASGY CCGKCTCTCT TGTGCCCTAG CAGATTCCGT CGCTTCTTCC GGAGCCGTAC 60 TCATACCGC CCCGCTCGCG GGCGGCCGCG RGGCTTGCTG GGAAGAGAGG CGAACCAGGT 120 ACCTTTCAA GGACCCAGAA GTAGGGTTTT GGCCTAGGTA ACGGGGCAGA G ATG TGG 177 Met Trp  TO GAG ATT CTC CCC GGA CTC TCC GTC ATG GGC GTG TGC TTG TTG ATT 225	(ix)	<ul><li>(A) NAME/KEY: other</li><li>(B) LOCATION: 114153</li><li>(C) IDENTIFICATION METH</li></ul>	identity 95 region 948 id C15963	
GOSCGASGY COGRETETT TGTGCCCTAG CAGATTCCGT CGCTTCTTCC GGAGCCGTAC 60 TOGTACOGC CCCGCTCGCG GGCGGCCGCG RGCCTTGCTG GGAAGAGAGG CGAACCAGGT 120 ACCTTTCAA GGACCCAGAA GTAGGGTTTT GGCCTAGGTA ACGGGGCAGA G ATG TGG 177 Met Trp TO GAG ATT CTC CCC GGA CTC TCC GTC ATG GGC GTG TGC TTG TTG ATT 225	(ix)	(A) NAME/KEY: sig_pepti (B) LOCATION: 172243 (C) IDENTIFICATION METH	OD: Von Heijne matrix score 5.5	
TOGTACOGO COCGOTOGOG GGCGGCCGCG RGGCTTGCTG GGAAGAGAG CGAACCAGGT 120  AMOUTTTCAA GGACCCAGAA GTAGGGTTTT GGCCTAGGTA ACGGGGCAGA G ATG TGG 177  Met Trp  TO GAG ATT CTC CCC GGA CTC TCC GTC ATG GGC GTG TGC TTG TTG ATT 225	(xi)	SEQUENCE DESCRIPTION: SE	CQ ID NO: 221:	
MYSTTTCAA GGACCCAGAA GTAGGGTTTT GGCCTAGGTA ACGGGGCAGA G ATG TGG 177 Met Trp  TO GAG ATT CTC CCC GGA CTC TCC GTC ATG GGC GTG TGC TTG TTG ATT 225	GCGCGASGY	CCGKCTCTCT TGTGCCCTAG CA	AGATTCCGT CGCTTCTTCC GGAGCCGTAC	60
Met Trp TO GAG ATT CTC CCC GGA CTC TCC GTC ATG GGC GTG TGC TTG TTG ATT 225	STORTACOGO	CCCGCTCGCG GGCGGCCGCG RO	GGCTTGCTG GGAAGAGAGG CGAACCAGGT	120
	AACTTTTVA	GGACCCAGAA GTAGGGTTTT GG		177
				225

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WO 99/06552 216 -20 -15 -10 CCA GGA CTG GCT ACT GCG TGC ATC CGG 252 Pro Gly Leu Ala Thr Ala Cys Ile Arg -5 (2) INFORMATION FOR SEQ ID NO: 222: (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 167 base pairs (B) TYPE: NUCLEIC ACID (C) STRANDEDNESS: DOUBLE (D) TOPOLOGY: LINEAR (ii) MOLECULE TYPE: CDNA (vi) ORIGINAL SOURCE: (A) ORGANISM: Homo Sapiens (F) TISSUE TYPE: Brain (ix) FEATURE: (A) NAME/KEY: other (B) LOCATION: complement(2..103) (C) IDENTIFICATION METHOD: blastn (D) OTHER INFORMATION: identity 98 region 48..149 id AA126155 est (ix) FEATURE: (A) NAME/KEY: other (B) LOCATION: complement (98..143) (C) IDENTIFICATION METHOD: blastn (D) OTHER INFORMATION: identity 95 region 7..52 id AA126155 est (ix) FEATURE: (A) NAME/KEY: sig\_peptide (B) LOCATION: 30..95 (C) IDENTIFICATION METHOD: Von Heijne matrix (D) OTHER INFORMATION: score 5.5 seg LADPLXLFPFSEG/LP (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 222: ACTGCTCSTG GAGCTCTGCG CTGGTCTTC ATG CGC CCT AGC CCT CTT TCG GGG Met Arg Pro Ser Pro Leu Ser Gly -20

ATA CTG GCC GAC CCC CTC TKC CTT TTC CCC TTT AGT GAA GGC CTC CCC

Ile Leu Ala Asp Pro Leu Xaa Leu Phe Pro Phe Ser Glu Gly Leu Pro

CGT CGC CGC GCG GCT TCC CGG AGC CGA CTG CAG ACT CCC TCA GCC CGG

Arg Arg Arg Ala Ala Ser Arg Ser Arg Leu Gln Thr Pro Ser Ala Arg

10

-10

5

101

149

PCT/IB98/01236 WO 99/06552 217

TGT TOO COG CGT CCG GGG Cys Ser Pro Arg Pro Gly

167

- (2) INFORMATION FOR SEQ ID NO: 223:
  - (i) SEQUENCE CHARACTERISTICS:
    - (A) LENGTH: 350 base pairs
    - (8) TYPE: NUCLEIC ACID
    - (C) STRANDEDNESS: DOUBLE
    - (D) TOPOLOGY: LINEAR
  - (ii) MOLECULE TYPE: CDNA
  - (vi) ORIGINAL SOURCE:
    - (A) ORGANISM: Homo Sapiens
    - (F) TISSUE TYPE: Brain
  - (ix) FEATURE:
    - (A) NAME/KEY: other
    - (B) LOCATION: 40..352
    - (C) IDENTIFICATION METHOD: blastn
    - (D) OTHER INFORMATION: identity 96 region 30..342 id H15315
  - (ix) FEATURE:
    - (A) NAME/KEY: other
    - (B) LOCATION: 12..46
    - (C) IDENTIFICATION METHOD: blastn
    - (D) OTHER INFORMATION: identity 91 region 1..35

id H15315

est

- (ix) FEATURE:

  - (A) NAME/KEY: other (B) LOCATION: 77..300
  - (C) IDENTIFICATION METHOD: blastn
  - (D) OTHER INFORMATION: identity 96 region 1..224 id HUM427H08B

est

est

- (ix) FEATURE:
  - (A) NAME/KEY: other
  - (B) LOCATION: 22..134
  - (C) IDENTIFICATION METHOD: blastn
  - (D) OTHER INFORMATION: identity 9! region 3..115 id AA071651
- (ix) FEATURE:
  - (A) NAME/KEY: other
  - (B) LOCATION: 138..326
  - [7] IDENTIFICATION METHOD: blastn

(D) OTHER INFORMATION: identity 95 region 32..220

id R35596

est

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ı	1 X	1 5	r.A	ı u	RL.	

- (A) NAME/KEY: other
- (B) LOCATION: 65..111
- (C) IDENTIFICATION METHOD: blastn
- (D) OTHER INFORMATION: identity 91

region 1..47 id W55530

est

#### (ix) FEATURE:

- (A) NAME/KEY: sig\_peptide
- (B) LOCATION: 261..341
- (C) IDENTIFICATION METHOD: Von Heijne matrix
- (D) OTHER INFORMATION: score 5.4

seq SLMMAQXFIPAVA/KV

350

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 223:

AGGAGGGCTG GACAGCAGCT CAGCTCGCTA GCTGCGCGCT TCCCGGCACA GGCAGTGCCA 60

CTGCGCAGGT TGATCAGCGA AACAGCATCC ATTTTAATCT GCGGGGAGNN CCTGCCTTAC 120

CAGGGCGTTC TCTCCGCCCG CCGGTGGATG CTCCGCGCCT GCSCTCCGCA GCCTCGCTCA 180

GCAGTCCTGC GTTGGGGTCT GCGCCCTAGG ATGCACTGAG ATGGTACATC AGGATAACTG 240

CTCGTATCAG GCACAGAAAA ATG AGA GAG AGT CTA TCA DKS AGA AGT TGG CAC 293

Met Arg Glu Ser Leu Ser Xaa Arg Ser Trp His

-25

-20

TTG CCA GCT TCT TTG ATG GCC CAG GKA TTT ATA CCA GCT GTA GCA

Leu Pro Ala Ser Leu Met Met Ala Gln Xaa Phe Ile Pro Ala Val Ala

-15

-10

-5

AAA GTA GGA Lys Val Gly

## (2) INFORMATION FOR SEQ ID NO: 224:

- (i) SEQUENCE CHARACTERISTICS:
  - (A) LENGTH: 430 base pairs
  - (B) TYPE: NUCLEIC ACID
  - (C) STRANDEDNESS: DOUBLE
  - (D) TOPOLOGY: LINEAR
- (ii) MOLECULE TYPE: CDNA
- (vi) ORIGINAL SOURCE:
  - (A) ORGANISM: Homo Sapiens
  - (F) TISSUE TYPE: Brain
- (ix) FEATURE:

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219

(A) NAME/KEY: other
(B) LOCATION: 226..295
(C) IDENTIFICATION METHOD: blastn
(D) OTHER INFORMATION: identity 95

(ix) FEATURE:

(A) NAME/KEY: sig\_peptide

(B) LOCATION: 251..424

(C) IDENTIFICATION METHOD: Von Heijne matrix

(D) OTHER INFORMATION: score 5.4

seq LSLHLLATRACYG/IL

region 121..190 id W07343 est

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 224:

AACAGGTGGT TGCAGAAGTT TCGTGGTGTC GGGCGCGCGT CTGCACTGCA	60
GTTTGGGAGC GAGCAGTTTC CTGCCCAGGG ATGGGGGTCC TGGCTGCACT TCACGGGGGC	120
GGCCCTTTCG TTTCGCTCTG CGTGACAGGT CTCGCTTGAT TGGGTTTCTC ATGGGTSKCT	180
GGCGTTTCTA CGGCGCGGCT CTCACGGACT CAGGCCAGGC	240
ATTCTTCAAA ATG TCA GGT GTG GTA CCC ACA GCC CCT GAA CAG CCT GCA Met Ser Gly Val Val Pro Thr Ala Pro Glu Gln Pro Ala -55 -50	289
NGT GAA ATG GAA AAT CAA ACA AAA CCA CCA GAT CCA AGG CCT GAT GCT Xaa Glu Met Glu Asn Gln Thr Lys Pro Pro Asp Pro Arg Pro Asp Ala -45	337
CCT CCT GAA TAC AGT TCT CAT DBG TTT ACC AGG ACC CCC TGG AAA CAG Pro Pro Glu Tyr Ser Ser His Xaa Phe Thr Arg Thr Pro Trp Lys Gln -25 -15	385
CTG TCC CTC CAC CTA CTG GCT ACC AGA GCT TGC TAT GGG ATA CTA Leu Ser Leu His Leu Leu Ala Thr Arg Ala Cys Tyr Gly Ile Leu -10	430

## (2) INFORMATION FOR SEQ ID NO: 225:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 387 base pairs

(B) TYPE: NUCLEIC ACID

(C) STRANDEDNESS: DOUBLE

(D) TOPOLOGY: LINEAR

(ii) MOLECULE TYPE: CDNA

(vi) ORIGINAL SOURCE:

(A) ORGANISM: Homo Sapiens

(F) TISSUE TYPE: Brain

(ix) FEATURE:

(A) NAME/KEY: other

(B) LOCATION: complement(75..325)

220

(C) IDENTIFICATION METHOD: blastn
(D) OTHER INFORMATION: identity 100 region 82..332 id AA004751

est

## (ix) FEATURE:

(A) NAME/KEY: other

(B) LOCATION: complement (88..255)

(C) IDENTIFICATION METHOD: blastn

(D) OTHER INFORMATION: identity 97

region 153..320

id N27443

est

## (ix) FEATURE:

(A) NAME/KEY: other

(B) LOCATION: complement(18..105)

(C) IDENTIFICATION METHOD: blastn

(D) OTHER INFORMATION: identity 94

region 304..391

id N27443

est

#### (ix) FEATURE:

(A) NAME/KEY: other

(B) LOCATION: complement (258..325)

(C) IDENTIFICATION METHOD: blastn

(D) OTHER INFORMATION: identity 100

region 81..148

id N27443

est

## (ix) FEATURE:

(A) NAME/KEY: other

(B) LOCATION: complement(22..325)

(C) IDENTIFICATION METHOD: blastn

(D) OTHER INFORMATION: identity 99

region 80..383

id AA015608

est

## (ix) FEATURE:

(A) NAME/KEY: other

(B) LOCATION: complement (78..253)

(C) IDENTIFICATION METHOD: blastn

(D) OTHER INFORMATION: identity 99

region 165..340

id H09727

est

## (ix) FEATURE:

(A) NAME/KEY: other

(B) LOCATION: complement (253..285)

(C) IDENTIFICATION METHOD: blastn

(D) OTHER INFORMATION: identity 96

region 132..164

id H09727

est

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	NAME/KEI: othe				
(€)	LOCATION: comp	METHOD:	blastn		
(D)	OTHER INFORMAT	req id	jion 133 AA027099	360	
		est			
(ix) FEAT (A)	URE: NAME/KEY: othe	er			
	LOCATION: comp	•			
	OTHER INFORMA	TION: ide		3.0	
		id	AA027099	3 9	
		est	-		
(ix) FEAT (A)	URE: NAME/KEY: sig	peptide			
(8)	LOCATION: 139	369	Von Heiin	e matrix	
	OTHER INFORMA	TION: sc	ore 5.3		
			•	rrGrg/La	
(xi) SEQU	JENCE DESCRIPTI	ON: SEQ I	D NO: 225:		
AGAAACAGGG AGAA	IGAGGAA GGCTAGA	AGC CTGAG	CAAGT GAGG	GTAGAA CCTTTTGGGA	. 60
CTGGCCTTTG AAG	CTCTGGC CAGGGAT	GGG GTGGG	GGCCA AAAG	GACAGA GCCTGGTATG	120
TCTTCATAGT CAT	Met Trp A	Arg Tyr Gl		TGG GGG GTG ATC Trp Gly Val Ile	171
	<del>-</del>	-75		-70	
				CTG TTG GCC TCA Leu Leu Ala Ser	219
-65	-60		-55		
				ACA TGC ACC TCA Thr Cys Thr Ser	267
-50	-45	ro nap be	-40	-35	
				TTG AAT GAA TTG	319
Leu Gly Phe Va	1 Thr Arg Val 3 -30	I'rp Met Se -2		Leu Asn Glu Leu -20	
AGT TTG TAT TC	T AGA ACC TGG (	GTT TTT AG	DA TUT TTG	GTC TTT TTT TGT	36.
Ser Leu Tyr Se		Val Phe Ti -10	ır Cys Leu	Val Phe Phys Cys -5	
	A MCC TCG CTA	aaa			38
Phe Gly Leu Se	r Xaa Ser Leu				30
1	5				
(A) THEODIANCE	W Don and to "	0 000			

(2) INFORMATION FOR SEQ ID NO: 226:

(i) SEQUENCE CHARACTERISTICS:
 (A) LENGTH: 300 base pairs

(B) TYPE: NUCLEIC ACID
(C) STRANDEDNESS: DOUBLE

(D) TOPOLOGY: LINEAR

(ii) MOLECULE TYPE: CDNA

(vi) ORIGINAL SOURCE:

(A) ORGANISM: Homo Sapiens(F) TISSUE TYPE: Brain

(ix) FEATURE:

(A) NAME/KEY: other
(B) LOCATION: 123..295

(C) IDENTIFICATION METHOD: blastn

(D) OTHER INFORMATION: identity 97 region 121..293

id N78275

est

(ix) FEATURE:

(A) NAME/KEY: other
(B) LOCATION: 43..128

(C) IDENTIFICATION METHOD: blastn

(D) OTHER INFORMATION: identity 100

region 40..125

id N78275

est

(ix) FEATURE:

(A) NAME/KEY: other
(B) LOCATION: 19..295

(C) IDENTIFICATION METHOD: blastn

(D) OTHER INFORMATION: identity 99

region 4..280

id R35388

est

(ix) FEATURE:

(A) NAME/KEY: other

(B) LOCATION: 40..295

(C) IDENTIFICATION METHOD: blastn

(D) OTHER INFORMATION: identity 98

region 14..269

id W03418

est

(ix) FEATURE:

(A) NAME/KEY: other

(B) LOCATION: 29..283

(C) IDENTIFICATION METHOD: blastn

(D) OTHER INFORMATION: identity 98

region 27..281 id HSC29H041

est

(ix) FEATURE:

(A) NAME/KEY: other

(B) LOCATION: 49..266

(C) IDENTIFICATION METHOD: blastn

(D) OTHER INFORMATION: identity 96 region 78..295

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id R60376

.60

120 180 228

276

300

est
<pre>(ix) FEATURE:     (A) MAME/KEY: sig_peptide     (B) LOCATION: 184270     (C) IDENTIFICATION METHOD: Von Heijne matrix     (D) OTHER INFORMATION: score 5.2</pre>
(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 226:
AAGACTGCGC GGCCGTWGGG CGTGCAGCGG CGCCAGTCGG CGGACGAGGG GCCCCCGGGA
GTTGCTGGAC TGAGACATGA GCCTCCAACT GTGTGGTTGG GCTCGGTAGC ACATCGTGGG
ACTTGGGTGT GCGCCCACAG ATGGTTTGGC CCTGCAGTGA CCAGAGCAGC CCAAGCCGCC
ACC ATG GTG AAA TTG CTA GTG GCC AAA ATC CTG TGC ATG GTG GGC GTG Met Val Lys Leu Val Ala Lys Ile Leu Cys Met Val Gly Val -25 -20 -15
TTC TTC TTC ATG CTG CTC GGC TCC CTG CTC CCC GTG AAG ATC ATC GAG Phe Phe Phe Met Leu Leu Gly Ser Leu Leu Pro Val Lys Ile Ile Glu -10 -5 1
ACA GAT TTT GAG AAG GCC CCA GGG Thr Asp Phe Glu Lys Ala Pro Gly 5 10
(2) INFORMATION FOR SEQ ID NO: 227:  (i) SEQUENCE CHARACTERISTICS:  (A) LENGTH: 76 base pairs  (B) TYPE: NUCLEIC ACID  (C) STRANDEDNESS: DOUBLE
(D) TOPOLOGY: LINEAR
(ii) MOLECULE TYPE: CDNA
<pre>(vi) ORIGINAL SOURCE:     (A) ORGANISM: Homo Sapiens     (F) TISSUE TYPE: Brain</pre>
<pre>(ix) FEATURE:     (A) NAME/KEY: other     (B) LOCATION: complement(273)     (C) IDENTIFICATION METHOD: blastn     (D) OTHER INFORMATION: identity 98</pre>
<pre>(ix) FEATURE:     (A) NAME/KEY: other     (B) LOCATION: complement(273)     (C) IDENTIFICATION METHOD: blastn</pre>

(D) OTHER INFORMATION: identity 98

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region 37..108 id T89094 est

- (ix) FEATURE:
  - (A) NAME/KEY: sig\_peptide
  - (B) LOCATION: 11..61
  - (C) IDENTIFICATION METHOD: Von Heijne matrix
  - (D) OTHER INFORMATION: score 5.2

seq IMCLIGLKANASS/ET

76

- (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 227:
- ATCCTTTTGC ATG CCT GTT TCT ATC ATG TGC TTG ATA GGC CTC AAA GCT

  Met Pro Val Ser Ile Met Cys Leu Ile Gly Leu Lys Ala

  -15

  -10

  -5

AAT GCT TCC AGT GAA ACA CAC TCA GGG
Asn Ala Ser Ser Glu Thr His Ser Gly
1 5

- (2) INFORMATION FOR SEQ ID NO: 228:
  - (i) SEQUENCE CHARACTERISTICS:
    - (A) LENGTH: 125 base pairs
    - (B) TYPE: NUCLEIC ACID
    - (C) STRANDEDNESS: DOUBLE
    - (D) TOPOLOGY: LINEAR
  - (ii) MOLECULE TYPE: CDNA
  - (vi) ORIGINAL SOURCE:
    - (A) ORGANISM: Homo Sapiens
    - (F) TISSUE TYPE: Brain
  - (ix) FEATURE:
    - (A) NAME/KEY: other
    - (B) LOCATION: 11..120
    - (C) IDENTIFICATION METHOD: blastn
    - (D) OTHER INFORMATION: identity 100 region 1..110

id HSC3IG111

est

- (ix) FEATURE:
  - (A) NAME/KEY: sig\_peptide
  - (B) LOCATION: 48..98
  - (C) IDENTIFICATION METHOD: Von Heijne matrix
  - (D) OTHER INFORMATION: score 5.2

seq LLYLVLEKLVSRA/FQ

-15

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 228:

AGATACTAAT CCTTTAAAAA AGTGTAAATG GAGAAAAGTT ATATTTT ATG AAG GTT
Met Lys Val

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125

225 ATT TTG TTG TAT TTA GTA TTG GAA AAG TTG GTT TCC AGA GCA TTT CAG Ile Leu Leu Tyr Leu Val Leu Glu Lys Leu Val Ser Arg Ala Phe Gln ~5 AAT GTC GAA GCA CCA CAC GGG Asn Val Glu Ala Pro His Gly 5 (2) INFORMATION FOR SEQ ID NO: 229: (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 170 base pairs (B) TYPE: NUCLEIC ACID (C) STRANDEDNESS: DOUBLE (D) TOPOLOGY: LINEAR (ii) MOLECULE TYPE: CDNA (vi) ORIGINAL SOURCE: (A) ORGANISM: Homo Sapiens (F) TISSUE TYPE: Brain (ix) FEATURE: (A) NAME/KEY: other (B) LOCATION: 81..170 (C) IDENTIFICATION METHOD: blastn (D) OTHER INFORMATION: identity 97 region 54..143 id T09307 est (ix) FEATURE: (A) NAME/KEY: other (B) LOCATION: 29..81 (C) IDENTIFICATION METHOD: blastn (D) OTHER INFORMATION: identity 92 region 1..53 id T09307 est (ix) FEATURE: (A) NAME/KEY: other (B) LOCATION: 12..77 (C) IDENTIFICATION METHOD: blastn (D) OTHER INFORMATION: identity 98 region 1..66 id AA159859 est (ix) FEATURE: (A) NAME/KEY: other (B) LOCATION: 28..75 (C) IDENTIFICATION METHOD: blastn (D) OTHER INFORMATION: identity 95 region 1..48 id H13321 est

(A) NAME/KEY: other

(B) LOCATION: 15..75

(C) IDENTIFICATION METHOD: blastn

(D) OTHER INFORMATION: identity 93

region 10..70 id W02365

(ix) FEATURE:

(A) NAME/KEY: other

(B) LOCATION: 33..77

(C) IDENTIFICATION METHOD: blastn

(D) OTHER INFORMATION: identity 95

region 1..45 id AA113927

est

(ix) FEATURE:

(A) NAME/KEY: sig peptide

(B) LOCATION: 33..89

(C) IDENTIFICATION METHOD: Von Heijne matrix

(D) OTHER INFORMATION: score 5.1

seq LLLGGRVCXPSLA/VG

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 229:

AAGCCGAYYG CTGAAGGCTG GTTTGCGTCG AC ATG GCG GTT ACC CTG AGT CTC 5.3 Met Ala Val Thr Leu Ser Leu

-15

TTG CTG GGC GGG CGC GTT TGC SCG CCG TCA CTC GCT GTG GGT TCG CGA 101 Leu Leu Gly Gly Arg Val Cys Xaa Pro Ser Leu Ala Val Gly Ser Arg

CCC GGG GGG TGG CGG GCC CAG GCC CTA TTG GCC GGG AGC CGG ACC CCG Pro Gly Gly Trp Arg Ala Gln Ala Leu Leu Ala Gly Ser Arg Thr Pro 10

15

ATT CCG ACT GGG AAC CGG AGG

170

Ile Pro Thr Gly Asn Arg Arg 25

## (2) INFORMATION FOR SEQ ID NO: 230:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 263 base pairs

(B) TYPE: NUCLEIC ACID

(C) STRANDEDNESS: DOUBLE

(D) TOPOLOGY: LINEAR

(ii) MOLECULE TYPE: CDNA

(vi) ORIGINAL SOURCE:

(A) ORGANISM: Homo Sapiens

(F) TISSUE TYPE: Brain

(ix) FEATURE:

(A) NAME/KEY: other

#### PCT/IB98/01236 WO 99/06552 227

(P) LOCATION: 57..261 (C) IDENTIFICATION METHOD: blastn (b) OTHER INFORMATION: identity 97 region 40..244 id R59037 est (ix) FEATURE: (A) NAME/KEY: other (B) LOCATION: complement(184..237) (C) IDENTIFICATION METHOD: blastn (D) OTHER INFORMATION: identity 100 region 38..91 id R67654 est (ix) FEATURE: (A) NAME/KEY: sig\_peptide (B) LOCATION: 117..185 (C) IDENTIFICATION METHOD: Von Heijne matrix (D) OTHER INFORMATION: score 5.1 seq LLPELGVVTPAQG/PR (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 230:

60 AAGACCATCA ACTATGGAAA GGAGATCTAG GGAACACCGT CTTGAACCCG CCAGGGTTTT

GAGTCTCGGA CCCAGGAGAT CCAACCCTGA CCACCCTCCC AGGATGCAGC AGGGGG ATG 119

TTA AAT CAG ACT TCA GGA AGA ACT TCC TTG CTG CCT GAG TTA GGT GTC 167 Leu Asn Gln Thr Ser Gly Arg Thr Ser Leu Leu Pro Glu Leu Gly Val -20 -15 -10

GTC ACG CCT GCC CAG GGG CCA AGG AGG CGG GTT TGG TGC GGC CAC TCC 215 Val Thr Pro Ala Gln Gly Pro Arg Arg Arg Val Trp Cys Gly His Ser -5

AAG GCC AAA GCG AGA AAA TCT TAC TGC GCA CGC GCA ATA GAC TGC CAG 263 Lys Ala Lys Ala Arg Lys Ser Tyr Cys Ala Arg Ala Ile Asp Cys Gln 20 15

## (2) INFORMATION FOR SEQ ID NO: 231:

- (i) SEQUENCE CHARACTERISTICS:
  - (A) LENGTH: 430 base pairs
  - (B) TYPE: NUCLEIC ACID
  - (C) STRANDEDNESS: DOUBLE
  - (D) TOPOLOGY: LINEAR
- (ii) MOLECULE TYPE: CDNA
- (vi) ORIGINAL SOURCE:
  - (A) ORGANISM: Homo Sapiens
  - (F) TISSUE TYPE: Brain
- (IN) FEATURE:
  - (A) NAME/KEY: other

228

(B) LOCATION: 99..416(C) IDENTIFICATION METHOD: blastn

(D) OTHER INFORMATION: identity 99 region 1..318

id T31969 est

## (ix) FEATURE:

(A) NAME/KEY: other

(B) LOCATION: 49..334

(C) IDENTIFICATION METHOD: blastn

(D) OTHER INFORMATION: identity 99

region 2..287 id HSB03B072

est

#### (ix) FEATURE:

(A) NAME/KEY: other

(B) LOCATION: complement(2..57)

(C) IDENTIFICATION METHOD: blastn

(D) OTHER INFORMATION: identity 100

region 1..56 id W51830

est

#### (ix) FEATURE:

(A) NAME/KEY: sig\_peptide

(B) LOCATION: 26..262

(C) IDENTIFICATION METHOD: Von Heijne matrix

(D) OTHER INFORMATION: score 5

seq SFLGFSAPTPIQA/LT

## (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 231:

ATGTGATGAT CCGGAGGCTG GGGAG ATG ACA TCA GAA AAC CTG GTC CAA ACT

Met Thr Ser Glu Asn Leu Val Gln Thr

-75

GCT CCA AAA AAG AAG AAA AAT AAA GGG AAA AAA GGG TTG GAG CCT TCT
Ala Pro Lys Lys Lys Asn Lys Gly Lys Lys Gly Leu Glu Pro Ser
-70
-65
-55

CAG AGC ACT GCT GCC AAG GTG CCC AAA AAA GCG AAG ACA TGG ATT CCT 148
Gln Ser Thr Ala Ala Lys Val Pro Lys Lys Ala Lys Thr Trp Ile Pro
-50 -45 -40

GAA GTT CAT GAT CAG AAA GCA GAT GTG TCA GCT TGG AAG GAC CTG TTT 196
Glu Val His Asp Gln Lys Ala Asp Val Ser Ala Trp Lys Asp Leu Phe
-35 -30 -25

GTT CCC AGG CCG GTT CTC CGA GCA CTC AGC TTT CTA GGC TTC TCT GCA

Val Pro Arg Pro Val Leu Arg Ala Leu Ser Phe Leu Gly Phe Ser Ala

-20

-15

-10

CCC ACA CCA ATC CAA GCC CTG ACC TTG GCA CCT GCC ATC CGT GAC AAA 292
Pro Thr Pro Ile Gln Ala Leu Thr Leu Ala Pro Ala Ile Arg Asp Lys
-5 1 5 10

CTG GAC ATC CTT GGG GCT GCT GAG ACA GGA AGT GGG AAA ACT CTT GCC
Leu Asp Ile Leu Gly Ala Ala Glu Thr Gly Ser Gly Lys Thr Leu Ala

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229 2.0 15 25 TIT GCC ATC CCA ATG ATT CAT GCG GTG TTG CAG TGG CAG AAG AGG AAT 388 Phe Ala Ile Pro Met Ile His Ala Val Leu Gln Trp Gln Lys Arg Asn 35 GCT GCC CCT CCA AGT AAC ACC GAA GCA CCA CCT GGA GAG 430 Ala Ala Pro Pro Pro Ser Asn Thr Glu Ala Pro Pro Gly Glu 50 45 (2) INFORMATION FOR SEQ ID NO: 232: (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 252 base pairs (B) TYPE: NUCLEIC ACID (C) STRANDEDNESS: DOUBLE (D) TOPOLOGY: LINEAR (ii) MOLECULE TYPE: CDNA (vi) ORIGINAL SOURCE: (A) ORGANISM: Homo Sapiens (F) TISSUE TYPE: Brain (ix) FEATURE: (A) NAME/KEY: other (B) LOCATION: 1..37 (C) IDENTIFICATION METHOD: blastn (D) OTHER INFORMATION: identity 97 region 9..45 id W84513 est (ix) FEATURE: (A) NAME/KEY: sig\_peptide (B) LOCATION: 16..84 (C) IDENTIFICATION METHOD: Von Heijne matrix (D) OTHER INFORMATION: score 4.9 seq WHXLIFLTWACMA/RQ (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 232: AATCTTCTCC GCGCT ATG GCT GCG TTC GGC CGT CAG SCW TTS ART TGG CAC Met Ala Ala Phe Gly Arg Gln Xaa Xaa Xaa Trp His CKY CTG ATC CCC CTC ACC TGG GCC TGT ATG GCT AGG CAG ACT CCT CAT Xaa Leu Ile Pro Leu Thr Trp Ala Cys Met Ala Arg Gln Thr Pro His CTT GGA GAA CAG AGA AGG ACG ACA GCT TCT TTG TKG CGC AAA CTG ACT Leu Gly Glu Gin Arg Arg Thr Thr Ala Ser Leu Xaa Arg Lys Leu Thr

15

195

ACA GCC TCC AAT GGA GGG GTC ATT GAG GAG TTA TCT TGT GTK AGA TCC

The Ala Ser Ash Gly Gly Val IIa Glu Glu Leu Ser dys Val Arg Ser 30

10

2.5

AAT AAC TAT GTG CAG GAA CCA GAG TGC AGG AGG AAT CTT GTT CAG TGC
Asn Asn Tyr Val Gln Glu Pro Glu Cys Arg Arg Asn Leu Val Gln Cys
40
45
50

CTC CTC TGG Leu Leu Trp 55

252

#### (2) INFORMATION FOR SEO ID NO: 233:

- (i) SEQUENCE CHARACTERISTICS:
  - (A) LENGTH: 347 base pairs
  - (B) TYPE: NUCLEIC ACID
  - (C) STRANDEDNESS: DOUBLE
  - (D) TOPOLOGY: LINEAR
- (ii) MOLECULE TYPE: CDNA
- (vì) ORIGINAL SOURCE:
  - (A) ORGANISM: Homo Sapiens
  - (F) TISSUE TYPE: Brain
- (ix) FEATURE:
  - (A) NAME/KEY: other
  - (B) LOCATION: 44..187
  - (C) IDENTIFICATION METHOD: blastn
  - (D) OTHER INFORMATION: identity 96 region 1..144 id AA151232

est

- (ix) FEATURE:
  - (A) NAME/KEY: other
  - (B) LOCATION: 187..285
  - (C) IDENTIFICATION METHOD: blastn
  - (D) OTHER INFORMATION: identity 97 region 143..241 id AA151232

est

- (ix) FEATURE:
  - (A) NAME/KEY: other
  - (3) LOCATION: 314..349
  - (C) IDENTIFICATION METHOD: blastn
  - (D) OTHER INFORMATION: identity 100 region 272..307

id AA151232

est

- (ix) FEATURE:
  - (A) NAME/KEY: other
  - (3) LOCATION: 39..225
  - (C) IDENTIFICATION METHOD: blastn
  - (D) OTHER INFORMATION: identity 95 region 2..188

id AA040827

est

WO 99/06552 PCT/IB98/01236

(A) NAME/KEY: sig\_peptide (B) LOCATION: 144..314 (C) IDENTIFICATION METHOD: Von Heijne matrix (D) OTHER INFORMATION: score 4.9 seq GWFLSGCPHGSSA/TW (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 233: AATGGGGATG TTGAATTTGG AAATTGGAGG GGACGCTGGT GGWYKKATTG GGTGCAAGGA 60 GTTGGTGTTG ATGGAGGAGC AGGASRCCAG AGTCCCAGCC CTGGAACCGT TCAGAGTGGA GCAGGCACCA CCTGTAATCT ACT ATG TCC CTG ACT TCA TCT CCA AAG AAG AGG Met Ser Leu Thr Ser Ser Pro Lys Lys Arg AGG AGT ATT TGC TTC GAC AGG TTT TTA ATG CCC CAA AGC CAA AGT GGA 221 Arg Ser Ile Cys Phe Asp Arg Phe Leu Met Pro Gln Ser Gln Ser Gly -45 -40-35 CCC AGC TCT CTG GGA GAA AGT TAC AGA ACT GGG GTG GGC TTC CTC ATC 269 Pro Ser Ser Leu Gly Glu Ser Tyr Arg Thr Gly Val Gly Phe Leu Ile -30 -25CCC GAG GGA TGG TTC CTG AGC GGC TGC CCC CAT GGC TCC AGC GCT ACG Pro Glu Gly Trp Phe Leu Ser Gly Cys Pro His Gly Ser Ser Ala Thr TGG ACA AAG TGT CAA ACC TCA GCC TCT TTG 347 Trp Thr Lys Cys Gln Thr Ser Ala Ser Leu (2) INFORMATION FOR SEQ ID NO: 234: (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 227 base pairs (B) TYPE: NUCLEIC ACID (C) STRANDEDNESS: DOUBLE (D) TOPOLOGY: LINEAR (ii) MOLECULE TYPE: CDNA

(ix) FEATURE:

(vi) ORIGINAL SOURCE:

(A) NAME/KEY: other(B) LOCATION: 115..226

(A) ORGANISM: Homo Sapiens
(F) TISSUE TYPE: Brain

(C) IDENTIFICATION METHOD: blastn

(D) OTHER INFORMATION: identity 95 region 135..246 id HSC0GF021

est

(ix) FEATURE:

(A) NAME/KEY: sig\_peptide(B) LOCATION: 901.206

(C) IDENTIFICATION METHOD: Von Heijne matrix (D) OTHER INFORMATION: score 4.8

seq SLXFCLSPPPSPS/LR

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 234:

AAACCCCATA CCCCCTCCC ATCTTGTGAT CACCCTCATT ACCTCTTCTG GGCCCCCTGT

GGACCTGCGT TGACCCAGCA TGGGCTACA ATG GGG GAG TTG GGT AAT CGC TCC 113 Met Gly Glu Leu Gly Asn Arg Ser -35

CGT TGC ATC CTG TTT CTG TCT GAA AAC CCT TGT CTT TCT GAA TCC ATC 161 Arg Cys Ile Leu Phe Leu Ser Glu Asn Pro Cys Leu Ser Glu Ser Ile -30 -25

TTT CAG TCT CTS RCA TTC TGT CTT TCC CCT CCT CCT TCA CCT TCC CTC Phe Gln Ser Leu Xaa Phe Cys Leu Ser Pro Pro Ser Pro Ser Leu -15 -10 -5

CGT CCC TCT CCC TCA CGG 227 Arg Pro Ser Pro Ser Arg

### (2) INFORMATION FOR SEQ ID NO: 235:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 430 base pairs
- (B) TYPE: NUCLEIC ACID
- (C) STRANDEDNESS: DOUBLE
- (D) TOPOLOGY: LINEAR
- (ii) MOLECULE TYPE: CDNA
- (vi) ORIGINAL SOURCE:
  - (A) ORGANISM: Homo Sapiens
  - (F) TISSUE TYPE: Brain
- (ix) FEATURE:
  - (A) NAME/KEY: other
  - (B) LOCATION: 101..355
  - (C) IDENTIFICATION METHOD: blastn
  - (D) OTHER INFORMATION: identity 99 region 83..337 id AA057242

est

- (ix) FEATURE:
  - (A) NAME/KEY: other
  - (B) LOCATION: 57..101
  - (C) IDENTIFICATION METHOD: blastn
  - (D) OTHER INFORMATION: identity 100 region 40..84 id AA057242 est
- (ix) FEATURE:
  - (A) NAME/KEY: other

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(B) LOCATION: 357..400

(C) IDENTIFICATION METHOD: blastm

(D) OTHER INFORMATION: identity 100 region 338..381 id AA057242 est. (ix) FEATURE: (A) NAME/KEY: other (B) LOCATION: 18..51 (C) IDENTIFICATION METHOD: blastn (D) OTHER INFORMATION: identity 100 region 1..34 id AA057242 est (ix) FEATURE: (A) NAME/KEY: other (B) LOCATION: 400..431 (C) IDENTIFICATION METHOD: blastn (D) OTHER INFORMATION: identity 100 region 382..413 id AA057242 est (ix) FEATURE: (A) NAME/KEY: other (B) LOCATION: 84..218 (C) IDENTIFICATION METHOD: blastn (D) OTHER INFORMATION: identity 97 region 73..207 id R09808 est (ix) FEATURE: (A) NAME/KEY: other (B) LOCATION: 10..51 (C) IDENTIFICATION METHOD: blastn (D) OTHER INFORMATION: identity 100 region 1..42 id R09808 est (ix) FEATURE: (A) NAME/KEY: sig\_peptide (B) LOCATION: 98..376 (C) IDENTIFICATION METHOD: Von Heijne matrix (D) OTHER INFORMATION: score 4.7 seq VLLLRQXFAQAEK/WY (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 235: AATTITCYGT GGTCCAACTA CCCTCGGCGA TCCCAGGCTT GGCGGGGCAC CGCCTGGCCT 60 CTCCCGTTCC TTTAGGCTGC CGCCGCTGCC TGCCGCC ATG GCA GAG TTG GGC CTA 115 Met Ala Glu Leu Gly Leu -90 AAT GAG CAC CAT CAA AAT GAA GTT ATT AAT THT ATG CGT TTT GCT CGT Asn Glu His His Gln Asn Glu Val Ile Asn The Met Arg Phe Ali Arg 163

-85 -80 -75

TCA AAG AGA GGC TTG AGA CTC AAA ACT GTA GAT TCC TGC TTC CAA GAC

Ser Lys Arg Gly Leu Arg Leu Lys Thr Val Asp Ser Cys Phe Gln Asp

-70

-65

-60

CTC AAG GAG AGC AGG CTG GTG GAG GAC ACC TTC ACC ATA GAT GAA GTC
Leu Lys Glu Ser Arg Leu Val Glu Asp Thr Phe Thr Ile Asp Glu Val
-55 -45 -40

TCT GAA GTC CTC AAT GGA TTA CAA GCT GTG GTT CAT AGT GAG GTG GAA

Ser Glu Val Leu Asn Gly Leu Gln Ala Val Val His Ser Glu Val Glu

-35

-30

-25

TCT GAG CTC ATC AAC ACT GCC TAT ACC AAT GTG TTA CTT CTG CGA CAG

Ser Glu Leu Ile Asn Thr Ala Tyr Thr Asn Val Leu Leu Leu Arg Gln

-20

-15

-10

NTG TTT GCA CAA GCT GAG AAG TGG TAT CTT AAG CTA CAG ACA GAC ATC

Xaa Phe Ala Glu Lys Trp Tyr Leu Lys Leu Gln Thr Asp Ile

-5

1

5

TCT GAA CTT GAA AAC CGA GAA TTA TTA

Ser Glu Leu Glu Asn Arg Glu Leu Leu

10

15

430

#### (2) INFORMATION FOR SEQ ID NO: 236:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 344 base pairs

(B) TYPE: NUCLEIC ACID

(C) STRANDEDNESS: DOUBLE

(D) TOPOLOGY: LINEAR

#### (ii) MOLECULE TYPE: CDNA

(vi) ORIGINAL SOURCE:

(A) ORGANISM: Homo Sapiens

(F) TISSUE TYPE: Brain

#### (ix) FEATURE:

(A) NAME/KEY: other

(B) LOCATION: 20..231

(C) IDENTIFICATION METHOD: blastn

(D) OTHER INFORMATION: identity 99 region 1..212 id N33729

est

#### (ix) FEATURE:

(A) NAME/KEY: sig\_peptide

(B) LOCATION: 135..281

(C) IDENTIFICATION METHOD: Von Heijne matrix

(D) OTHER INFORMATION: score 4.6

seq SWAVGLLYAVAQG/SK

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 236:

AATTAGCGAG	GCCATGGG	GG AAAAAGTO	CTA ACTGGCGGAA	CTCCTGGGAA CTGGGGCGAT	60
GGGCTCTTAG	TATCGGAG	GA TTGGAGCO	CAT CTGATTTTA	CCTGAAATTC CTTAGTCTCT	120
CCTGTGTTGG				ACC TGG GCT TTC AGC Thr Trp Ala Phe Ser -40	170
	c Leu Ala	Leu Val As		CTG GGC AGT GCA CGT Leu Gly Ser Ala Arg -25	218
				GTT GGT CTT CTT TAT Val Gly Leu Leu Tyr -10	266
				CAA GAT GTC AAG CCT Gln Asp Val Lys Pro 10	314
		ACT GGC ACT Thr Gly Th			344

20

## (2) INFORMATION FOR SEQ ID NO: 237:

15

- (i) SEQUENCE CHARACTERISTICS:
  - (A) LENGTH: 419 base pairs
  - (B) TYPE: NUCLEIC ACID
  - (C) STRANDEDNESS: DOUBLE
  - (D) TOPOLOGY: LINEAR
- (ii) MOLECULE TYPE: CDNA
- (vi) ORIGINAL SOURCE:
  - (A) ORGANISM: Homo Sapiens
  - (F) TISSUE TYPE: Brain
- (ix) FEATURE:
  - (A) NAME/KEY: other
  - (B) LOCATION: 116..419
  - (C) IDENTIFICATION METHOD: blastn
  - (D) OTHER INFORMATION: identity 98

region 122..425

id W68799

est

- (ix) FEATURE:
  - (A) NAME/KEY: other
  - (B) LOCATION: 18..117
  - (C) IDENTIFICATION METHOD: blastn
  - (D) OTHER INFORMATION: identity 97 region 1..100 ia W63799

est

- (ix) FEATURE:
  - (A) NAME/KEY: other
  - (B) LOCATION: 18..209

(C) IDENTIFICATION METHOD: blastn
(D) OTHER INFORMATION: identity 93
region 1..192
id W49697

## (ix) FEATURE:

- (A) NAME/KEY: other
  (B) LOCATION: 199..290
- (C) IDENTIFICATION METHOD: blastn
- (D) OTHER INFORMATION: identity 95

region 183..274

id W49697

est

est

## (ix) FEATURE:

- (A) NAME/KEY: other
  (B) LOCATION: 291..367
- (C) IDENTIFICATION METHOD: blastn
- (D) OTHER INFORMATION: identity 97

region 276..352

id W49697

est

#### (ix) FEATURE:

- (A) NAME/KEY: other
- (B) LOCATION: 387..417
- (C) IDENTIFICATION METHOD: blastn
- (D) OTHER INFORMATION: identity 100

region 374..404

id W49697

est

## (ix) FEATURE:

- (A) NAME/KEY: other
- (B) LOCATION: 48..419
- (C) IDENTIFICATION METHOD: blastn
- (D) OTHER INFORMATION: identity 98

region 1..372

id AA149518

est

## (ix) FEATURE:

- (A) NAME/KEY: other
- (B) LOCATION: 171..414
- (C) IDENTIFICATION METHOD: blastn

(D) OTHER INFORMATION: identity 97

region 116..359

id W17032

est

#### (ix) FEATURE:

- (A) NAME/KEY: other
- (B) LOCATION: 57..174
- (C) IDENTIFICATION METHOD: blastn
- (D) OTHER INFORMATION: identity 97

region 1..118

id W17032

est .

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			(B) (C)	NAME LOCA IDEN OTHE	TION TIFI	: 78 CATI	38 ON M	ETHO N:	D: b iden regi id W est	tity on 1	98 30	9				
	(i	x) F	(B) (C)	RE: NAME LOCA IDEN OTHE	TION TIFI	: 38 CATI	64 ON M	ETHO N:	D: b iden regi id W est	tity on 3	100 10					
	(i	×) F	(B) (C)	RE: NAME LOCA IDEN OTHE	TION TIFI	: 18 CATI	03 ON M	83 ETHO	D: V scor	e 4.	6		trix G/LV			
	( x	i) S	EQUE	NCE	DESC	RIPT	ION:	SEÇ	) ID	NO:	237:					
AAGA	.CAGG	GTG C	GGT <i>P</i>	CTCG	G GA	AGCI	GGAC	G CGC	GCCG	GCG	GTGC	AGTO	CAC G	GGGG	AGCGA	60
GGCC	TGCT	rgg c	GCTTC	GCAF	AC GA	\GGG <i>F</i>	CTCC	GCC	CTCGC	SAGG	CGAC	CCAC	SAC C	ACAC	AGACA	120
CTGG	GTCA	AAG (	GAGTA	AAGCA	AG AC	GATA	AAACA	A ACT	rggaj	AGGA	GAGO	CAAGO	CAC A	AAGI	CATC	179
			GCG Ala -65													227
			AGC Ser													275
CAC His	ATC Ile -35	CAC His	AGA Arg	GCA Ala	GAG Glu	ATC Ile -30	TCA Ser	AAG Lys	ATT Ile	ATG Met	CGA Arg -25	GAA Glu	TGT Cys	CAG Gln	GAA Glu	323
			TGG Trp													371
			GGA Gly						Tyr							419

## (2) INFORMATION FOR SEQ ID NO: 238:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 274 base pairs
  (B) TYPE: NUCLEIC ACID
  (C) STRANDEDNESS: DOUBLE

(D) TOPOLOGY: LINEAR

(ii) MOLECULE TYPE: CDNA

#### (vi) ORIGINAL SOURCE:

- (A) ORGANISM: Homo Sapiens
- (F) TISSUE TYPE: Brain

#### (ix) FEATURE:

- (A) NAME/KEY: other
- (B) LOCATION: complement (37..269)
- (C) IDENTIFICATION METHOD: blastn
- (D) OTHER INFORMATION: identity 99

region 2..234 id AA147071

est

#### (ix) FEATURE:

- (A) NAME/KEY: other
- (B) LOCATION: complement(2..31)
- (C) IDENTIFICATION METHOD: blastn
- (D) OTHER INFORMATION: identity 93

region 239..268 id AA147071

est

#### (ix) FEATURE:

- (A) NAME/KEY: other
- (B) LOCATION: complement (37..269)
- (C) IDENTIFICATION METHOD: blastn
- (D) OTHER INFORMATION: identity 99

region 58..290

id H98153

est

## (ix) FEATURE:

- (A) NAME/KEY: other
- (B) LOCATION: complement(2..31)
- (C) IDENTIFICATION METHOD: blastn
- (D) OTHER INFORMATION: identity 93

region 295..324

id H98153

est

#### (ix) FEATURE:

- (A) NAME/KEY: other
- (B) LOCATION: complement (37..269)
- (C) IDENTIFICATION METHOD: blastn
- (D) OTHER INFORMATION: identity 98

region 59..291

id N49401

est

#### (ix) FEATURE:

- (A) NAME/KEY: other
- (B) LOCATION: complement(2..31)
- (C) IDENTIFICATION METHOD: blastn
- (D) OTHER INFORMATION: identity 93

region 296..325

id N49401

est

PCT/IB98/01236 WO 99/06552 239 (ix) FEATURE: (A) NAME/KEY: other (B) LOCATION: complement (87..269) (C) I-DENTIFICATION METHOD: blastn (D) OTHER INFORMATION: identity 99 region 37..219 id N80022 est (ix) FEATURE: (A) NAME/KEY: sig\_peptide (B) LOCATION: 62..268 (C) IDENTIFICATION METHOD: Von Heijne matrix (D) OTHER INFORMATION: score 4.5 seq FILSLCVLCIVLT/TG

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 238:

AATTAAGTCA KDATACAAAT CAGCACAGAT AACGDMAATG TTTCCAATAT WWTAAAATGT A ATG TTA CTT ATG AAA AGT ATT TTG CTT AAG GTT GTG TGT GTA TTG TGT Met Leu Leu Met Lys Ser Ile Leu Leu Lys Val Val Cys Val Leu Cys -65 -60 ATA TAC CTC AAG TTC AAG TTA ATG GCA TTG ATT TAT GTT CCA GAC AAA 157 Ile Tyr Leu Lys Phe Lys Leu Met Ala Leu Ile Tyr Val Pro Asp Lys -50 -45 AAT AAC ACA AAT AAT AAT ATC CTT CGT TAT AAC CAC AAT GAG ATA AGT 205 Asn Asn Thr Asn Asn Asn Ile Leu Arg Tyr Asn His Asn Glu Ile Ser ATT GGC ATT AGT GTT CAG TGC CAT TTT ATA CTT TCT CTC TGT GTT CTC Ile Gly Ile Ser Val Gln Cys His Phe Ile Leu Ser Leu Cys Val Leu -10-15 274 TGT ATT GTA CTA ACC ACT GGG Cys Ile Val Leu Thr Thr Gly -5

#### (2) INFORMATION FOR SEQ ID NO: 239:

- (i) SEQUENCE CHARACTERISTICS:
  - (A) LENGTH: 249 base pairs
  - (B) TYPE: NUCLEIC ACID
  - (C) STRANDEDNESS: DOUBLE
  - (D) TOPOLOGY: LINEAR
- (ii) MOLECULE TYPE: CDNA
- (vi) ORIGINAL SOURCE:
  - (A) ORGANISM: Homo Sapiens
  - (F) TISSUE TYPE: Brain
- (ix) FEATURE:
  - (A) NAME/KEY: other
  - (B) LOCATION: 100..249

(C) IDENTIFICATION METHOD: blastn (D) OTHER INFORMATION: identity 94

region 20..169

id N41898

est

i	ix	۱ E	F A	וויד	RE:
и	1 X	, ,	ဌ	ΙU	RE:

(A) NAME/KEY: other

(B) LOCATION: 113..249

(C) IDENTIFICATION METHOD: blastn

(D) OTHER INFORMATION: identity 94

region 38..174

id H69272

est

### (ix) FEATURE:

(A) NAME/KEY: sig\_peptide

(B) LOCATION: 100..147

(C) IDENTIFICATION METHOD: Von Heijne matrix

(D) OTHER INFORMATION: score 4.5

seq RLLLRRFLASVIS/RK

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 239:

AGTTATGTAC GTTCCCCCC CCGAGGAAGT GAYGACAGGC GTGCCCTTGA CAGGCAGGGA 60

GGGCTAGGCT GTGCATCCCT CCGCTCGCAT TGCAGGGAG ATG GCT CAG CGA CTT 114 Met Ala Gln Arg Leu

-15

210

249

CTT CTG AGG AGG TTC CTG GCC TCT GTC ATC TCC AGG AAG CCC TCT CAG Leu Leu Arg Arg Phe Leu Ala Ser Val Ile Ser Arg Lys Pro Ser Gln -10 -5

GGT CAG TGG CCA CCC CTC ACT TCC AGA GCC CTG CAG ACC CCA YAA TGC

Gly Gln Trp Pro Pro Leu Thr Ser Arg Ala Leu Gln Thr Pro Xaa Cys 10 15

AGT YCT GGT GGC CTG ACT GTA ACA CCC AAC CCA AGC CGG Ser Xaa Gly Gly Leu Thr Val Thr Pro Asn Pro Ser Arg 25 30

## (2) INFORMATION FOR SEQ ID NO: 240:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 310 base pairs

(B) TYPE: NUCLEIC ACID

(C) STRANDEDNESS: DOUBLE

(D) TOPOLOGY: LINEAR

(ii) MOLECULE TYPE: CDNA

(vi) ORIGINAL SOURCE:

(A) ORGANISM: Homo Sapiens

(F) TISSUE TYPE: Brain

(ix) FEATURE:

(A) NAME/KEY: other

241 (B) LOCATION: 51..209 (C) IDENTIFICATION METHOD: blastn (D) OTHER INFORMATION: identity 99 region 49..207 id N56053 est (ix) FEATURE: (A) NAME/KEY: other (B) LOCATION: 2..54 (C) IDENTIFICATION METHOD: blastn (D) OTHER INFORMATION: identity 96 region 1..53 id N56053 est (ix) FEATURE: (A) NAME/KEY: other (B) LOCATION: 211..246 (C) IDENTIFICATION METHOD: blastn (D) OTHER INFORMATION: identity 100 region 208..243 id N56053 (ix) FEATURE: (A) NAME/KEY: other (B) LOCATION: 275..307 (C) IDENTIFICATION METHOD: blastn (D) OTHER INFORMATION: identity 96 region 270..302 id N56053 est (ix) FEATURE: (A) NAME/KEY: other (B) LOCATION: 51..178 (C) IDENTIFICATION METHOD: blastn (D) OTHER INFORMATION: identity 98 region 44..171 id R59444 est (ix) FEATURE: (A) NAME/KEY: other (B) LOCATION: 212..275 (C) IDENTIFICATION METHOD: blastn (D) OTHER INFORMATION: identity 100 region 203..266 id R59444 est (ix) FEATURE: (A) NAME/KEY: other (3) LOCATION: 7..54 (C) IDENTIFICATION METHOD: blastn

(D) OTHER INFORMATION: identity 95

region 1..48 id R59444 est

#### (ix) FEATURE:

(A) NAME/KEY: other

(B) LOCATION: 274..308

(C) IDENTIFICATION METHOD: blastn

(D) OTHER INFORMATION: identity 100

region 266..300

id R59444

#### (ix) FEATURE:

(A) NAME/KEY: other

(B) LOCATION: 178..209

(C) IDENTIFICATION METHOD: blastn

(D) OTHER INFORMATION: identity 100

region 170..201

id R59444

est

#### (ix) FEATURE:

(A) NAME/KEY: other

(B) LOCATION: 51..178

(C) IDENTIFICATION METHOD: blastn

(D) OTHER INFORMATION: identity 98

region 45..172 id AA156837

est

#### (ix) FEATURE:

(A) NAME/KEY: other

(B) LOCATION: 178..246

(C) IDENTIFICATION METHOD: blastn

(D) OTHER INFORMATION: identity 100

region 171..239

id AA156837

est

## (ix) FEATURE:

(A) NAME/KEY: other

(3) LOCATION: 247..308

(C) IDENTIFICATION METHOD: blastn

(D) OTHER INFORMATION: identity 100

region 239..300

id AA156837

est

### (ix) FEATURE:

(A) NAME/KEY: other

(B) LOCATION: 6..54

(C) IDENTIFICATION METHOD: blastn

(D) OTHER INFORMATION: identity 95

region 1..49

id AA156837

est

## (ix) FEATURE:

(A) NAME/KEY: other

(B) LOCATION: 51..178

(C) IDENTIFICATION METHOD: blastn

(D) OTHER INFORMATION: identity 99

region 56..183

id N88392

est

```
(ix) FEATURE:
```

- (A) NAME/KEY: other
- (B) LOCATION: 13..54
- (C) IDENTIFICATION METHOD: blastn
- (D) OTHER INFORMATION: identity 95

region 19..60 id N88392

est

#### (ix) FEATURE:

- (A) NAME/KEY: other
- (B) LOCATION: 247..285
- (C) IDENTIFICATION METHOD: blastn
- (D) OTHER INFORMATION: identity 100

region 249..287

id N88392

est

#### (ix) FEATURE:

- (A) NAME/KEY: other
- (B) LOCATION: 211..246
- (C) IDENTIFICATION METHOD: blastn
- (D) OTHER INFORMATION: identity 100

region 214..249

id N88392

est

## (ix) FEATURE:

- (A) NAME/KEY: other
- (B) LOCATION: 179..209
- (C) IDENTIFICATION METHOD: blastn
- (D) OTHER INFORMATION: identity 100

region 183..213

id N88392 est

#### (ix) FEATURE:

- (A) NAME/KEY: other
- (B) LOCATION: 7..209
- (C) IDENTIFICATION METHOD: blastn
- (D) OTHER INFORMATION: identity 98

region 1..203

id R18752

est

#### (ix) FEATURE:

- (A) NAME/KEY: other
- (B) LOCATION: 211..246
- (C) IDENTIFICATION METHOD: blastn
- (D) OTHER INFORMATION: identity 100

region 204..239 id R18752

est

- (A) NAME/KEY: sig\_peptide(B) LOCATION: 2...232
- (C) IDENTIFICATION METHOD: Von Heijne matrix
- (D) OTHER INFORMATION: score 4.4

# seq FEARIALLPLLQA/ET

# (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 240:

A ATG GCG GCG TCA AAG GTG AAG CAG GAC ATG CCT CCR MCG GGG GGC TAT Met Ala Ala Ser Lys Val Lys Gln Asp Met Pro Pro Xaa Gly Gly Tyr -75 -70 -65	49
GGG CCC ATC GAC TAC AAA CGG AAC TTG CCG CGT CGA GGA CTG TCG GGC Gly Pro Ile Asp Tyr Lys Arg Asn Leu Pro Arg Arg Gly Leu Ser Gly -60 -55	97
TAC AGC ATG CTG GCC ATA GGG ATT GGA ACC CTG ATC TAC GGG CAC TGG Tyr Ser Met Leu Ala Ile Gly Ile Gly Thr Leu Ile Tyr Gly His Trp -45 -35 -30	145
AGC ATA ATG AAG TGG AAC CGT GAG CGC AGG CGC CTA CAA ATC GAG GAC Ser Ile Met Lys Trp Asn Arg Glu Arg Arg Arg Leu Gln Ile Glu Asp -25 -20 -15	193
TTC GAG GCT CGC ATC GCG CTG TTG CCA CTG TTA CAG GCA GAA ACC GAC Phe Glu Ala Arg Ile Ala Leu Leu Pro Leu Leu Gln Ala Glu Thr Asp -10 -5 1	241
CGG AGG ACC TTG CAG ATG CTT CGG GAG AAC CTG GAG GAG GAG GCC ATC Arg Arg Thr Leu Gln Met Leu Arg Glu Asn Leu Glu Glu Ala Ile 5	289
ATC ATG AAG GAC GTG CCC GGA Ile Met Lys Asp Val Pro Gly	310

## (2) INFORMATION FOR SEQ ID NO: 241:

20

(i) SEQUENCE CHARACTERISTICS:

25

- (A) LENGTH: 388 base pairs
- (B) TYPE: NUCLEIC ACID
- (C) STRANDEDNESS: DOUBLE
- (D) TOPOLOGY: LINEAR
- (ii) MOLECULE TYPE: CDNA
- (vi) ORIGINAL SOURCE:
  - (A) ORGANISM: Homo Sapiens
  - (F) TISSUE TYPE: Brain
- (ix) FEATURE:
  - (A) NAME/KEY: other
  - (B) LOCATION: 93..257
  - (C) IDENTIFICATION METHOD: blastn
  - (D) OTHER INFORMATION: identity 99 region 103..267 id H87397 est
- (ix) FEATURE:
  - (A) NAME/KEY: sig\_peptide
  - (9) LOCATION: 159..319

(C) IDENTIFICATION METHOD: Von Heijne matrix (D) OTHER INFORMATION: score 4.3

seq LLSLAILSHISTP/GC

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 241:

AGACAAAGAG AAGGCAAAAT SAGTTTGTGT CCCTGAGTTG CTAAGTGGAG AAGAAACGTC 60 CACCAACCAG GAAACACCTG CCTCCAACTG TTAATAGGTC TGTGAAATGT GCTTTGTTTC 120 TGGTCAGCAT GGACACCCGC TTTAATAGTG GCTTCAG ATG AGG CAC CTT GTG ACA Met Arg His Leu Val Thr GAG GAG CTC TTC CCC TGC AGC AAC CTT GAA GAT GTT GTG GAA GAC AAT Glu Glu Leu Phe Pro Cys Ser Asn Leu Glu Asp Val Val Glu Asp Asn 223 AGC CAT TCT TAC TTC ACT CTG AGG ATC ACG ATG GCG TGC AAG GGT GTG Ser His Ser Tyr Phe Thr Leu Arg Ile Thr Met Ala Cys Lys Gly Val 271 -25 CCA AGC ACA TTG CTA TCT TTG GCC ATT CTC TCT CAC ATT AGT ACA CCT Pro Ser Thr Leu Leu Ser Leu Ala Ile Leu Ser His Ile Ser Thr Pro 319 -10 -5 GGA TGT GAA TGG CAC GTT ATC TAT GTA AGC AGT BAT GGT CTC TAT CTT Gly Cys Glu Trp His Val Ile Tyr Val Ser Ser Xaa Gly Leu Tyr Leu 367 10 1.5 GTG GTA GAA ATG ACA GAC CGG Val Val Glu Met Thr Asp Arg

388

(2) INFORMATION FOR SEQ ID NO: 242:

20

- (i) SEQUENCE CHARACTERISTICS:
  - (A) LENGTH: 391 base pairs
  - (B) TYPE: NUCLEIC ACID
  - (C) STRANDEDNESS: DOUBLE
  - (D) TOPOLOGY: LINEAR
- (ii) MOLECULE TYPE: CDNA
- (vi) ORIGINAL SOURCE:
  - (A) ORGANISM: Homo Sapiens
  - (F) TISSUE TYPE: Brain
- (ix) FEATURE:
  - (A) NAME/KEY: other
  - (B) LOCATION: 108..392
  - (C) IDENTIFICATION METHOD: blastn
  - (D) OTHER IMFORMATION: identity 98 region 104..388

id T08101 est

(13) FEATURE:

(A) NAME/KEY: other

(B) LOCATION: 32..110

(C) IDENTIFICATION METHOD: blastn

(D) OTHER INFORMATION: identity 98

region 1..79 id T08101

est

#### (ix) FEATURE:

(A) NAME/KEY: other

(B) LOCATION: 108..392

(C) IDENTIFICATION METHOD: blastn

(D) OTHER INFORMATION: identity 98

region 39..323

id T27149

est

## (ix) FEATURE:

(A) NAME/KEY: other

(B) LOCATION: 113..392

(C) IDENTIFICATION METHOD: blastn

(D) OTHER INFORMATION: identity 98

region 30..309

id H06555

est

#### (ix) FEATURE:

(A) NAME/KEY: other

(B) LOCATION: 108..316

(C) IDENTIFICATION METHOD: blastn

(D) OTHER INFORMATION: identity 99

region 90..298

id HSC3CC081

est

## (ix) FEATURE:

(A) NAME/KEY: other

(B) LOCATION: 60..110

(C) IDENTIFICATION METHOD: blastn

(D) OTHER INFORMATION: identity 94

region 15..65

id HSC3CC081

est

#### (ix) FEATURE:

(A) NAME/KEY: other

(B) LOCATION: 105..316

(C) IDENTIFICATION METHOD: blastn

(D) OTHER INFORMATION: identity 99

region 58..269

id T74159

est

#### (ix) FEATURE:

(A) NAME/KEY: other

(B) LOCATION: 76..105

(C) IDENTIFICATION METHOD: blastn

(D) OTHER INFORMATION: identity 93

region 5..34

id T74159

est

<ul> <li>(1x) FEATURE:</li> <li>(A) NAME/KEY: sig_peptide</li> <li>(B) LOCATION: 152379</li> <li>(C) PDENTIFICATION METHOD: Von Heijne matrix</li> <li>(D) OTHER INFORMATION: score 4.3</li> </ul>													
seq FRLLXVFAYGTYA/DY  (xi) SEQUENCE DESCRIPTION: GRO TO WE													
(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 242:													
AAGTGGCCAG AGCGACTCTT CAGGGAGGTG GCAGGAAAGG CTTGGAACAG CTGCCGGAGG	60												
TGACGGAGCG GCGGCCCCGC CCGGTGCGCT GGAGGTCGAA GCTTCCAGCT CTGGACATCC	120												
TGAGCCCAAG TCCCCCACAC TCAGTGCAGT G ATG AGT GCG GAA GTG AAG GTG  Met Ser Ala Glu Val Lys Val  -75  -70	172												
ACA GGG CAG AAC CAG GAG CAA TTT CTG CTC CTA GCC AAG TCG GCC AAG Thr Gly Gln Asn Gln Glu Gln Phe Leu Leu Leu Ala Lys Ser Ala Lys -65 -60 -55	220												
GGG GCA GCG CTG GCC ACA CTC ATC CAT CAG GTG CTG GAG GCC CCT GGT Gly Ala Ala Leu Ala Thr Leu Ile His Gln Val Leu Glu Ala Pro Gly -50 -45	268												
GTC TAC GTG TTT GGA GAA CTG CTG GAC ATG CCC AAT GTT AGA GAG CTG Val Tyr Val Phe Gly Glu Leu Leu Asp Met Pro Asn Val Arg Glu Leu -35 -25	316												
GCT GAG AGT NAC TTT GCC TCT ACC TTC CGG CTG CTC AMA GTG TTT GCT Ala Glu Ser Xaa Phe Ala Ser Thr Phe Arg Leu Leu Xaa Val Phe Ala -20 -15 -10	364												
TAT GGG ACA TAC GCT GAC TAC TWA GCT Tyr Gly Thr Tyr Ala Asp Tyr Xaa Ala -5	391												
(2) INFORMATION FOR SEQ ID NO: 243:  (i) SEQUENCE CHARACTERISTICS:  (A) LENGTH: 299 base pairs  (B) TYPE: NUCLEIC ACID  (C) STRANDEDNESS: DOUBLE  (D) TOPOLOGY: LINEAR													
(ii) MOLECULE TYPE: CDNA													
<pre>(vi) ORIGINAL SOURCE:     (A) ORGANISM: Homo Sapiens     (F) TISSUE TYPE: Brain</pre>													
(ix) FEATURE:  (A) NAME/KEY: other  (B) LOCATION: 47248  (C) IDENTIFICATION METHOD: blastn  (D) OTHER INFORMATION: identity 97  region 15216													

id HUM429E03B

#### (ix) FEATURE:

- (A) NAME/KEY: other
- (B) LOCATION: 244..299
- (C) IDENTIFICATION METHOD: blastn
- (D) OTHER INFORMATION: identity 94

region 211..266

id HUM429E03B

est

#### (ix) FEATURE:

- (A) NAME/KEY: other
- (B) LOCATION: 133..299
- (C) IDENTIFICATION METHOD: blastn
- (D) OTHER INFORMATION: identity 97

region 107..273

id T80259

est

## (ix) FEATURE:

- (A) NAME/KEY: other
- (B) LOCATION: 47..139
- (C) IDENTIFICATION METHOD: blastn
- (D) OTHER INFORMATION: identity 92

region 22..114

id T80259

est

#### (ix) FEATURE:

- (A) NAME/KEY: other
- (B) LOCATION: 48..292
- (C) IDENTIFICATION METHOD: blastn
- (D) OTHER INFORMATION: identity 94

region 1..245

id T31768

est

#### (ix) FEATURE:

- (A) NAME/KEY: other
- (B) LOCATION: 111..299
- (C) IDENTIFICATION METHOD: blastn
- (D) OTHER INFORMATION: identity 94

region 47..235

id N32697

est

#### (ix) FEATURE:

- (A) NAME/KEY: other
- (B) LOCATION: 64..106
- (C) IDENTIFICATION METHOD: blastn
- (D) OTHER INFORMATION: identity 97

region 1..43

id N32697

est

- (A) NAME/KEY: other
- (B) LOCATION: 74..299
- (C) IDENTIFICATION METHOD: blastn

WO 99/06552 PCT/IB98/01236

(D) OTHER INFORMATION: identity 94 region 1..226 id N44613 est

(1x) FEATURE:

(A) NAME/KEY: sig\_peptide (B) LOCATION: 165..266

(C) IDENTIFICATION METHOD: Von Heijne matrix

(D) OTHER INFORMATION: score 4.3

seq QLFAFLNLLPVEA/DI

(x1) SEQUENCE DESCRIPTION: SEQ ID NO: 243:

ACTTCCGCTT CGCCTAGGTG TTGTCGTCCC TGCTAGTACT CCGGGCTGGG GGTCGGTGCG 60 GATATTCAGT CATGAAATCA SGGTAGGGAC TTCTCCCGCA GCGACGCGCC TGGCAAGACT 120 GTTTGTGTWG CGGGGGCCGG ACTTCAAGGT GATTTTACAA CGAG ATG CTG CTC TCC 176 Met Leu Leu Ser ATA GGG ATG CTC ATG CTG TCA GCC ACA CAA GTS TAS ACC ATC TTG AST 224 Ile Gly Met Leu Met Leu Ser Ala Thr Gln Val Xaa Thr Ile Leu Xaa -30 -25 -20 GTC CAG CTC TTT GCA TTC TTA AAC CTA CTG CCT GTA GAA GCA GAC ATT Val Gln Leu Phe Ala Phe Leu Asn Leu Leu Pro Val Glu Ala Asp Ile -10 KTA GCA TAT AAC TTT GAA AAT GCA TCT 299 Xaa Ala Tyr Asn Phe Glu Asn Ala Ser 5 10

#### (2) INFORMATION FOR SEQ ID NO: 244:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 312 base pairs

(B) TYPE: NUCLEIC ACID

(C) STRANDEDNESS: DOUBLE

(D) TOPOLOGY: LINEAR

(ii) MOLECULE TYPE: CDNA

(vi) ORIGINAL SOURCE:

(A) ORGANISM: Homo Sapiens

(F) TISSUE TYPE: Brain

(1x) FEATURE:

(A) NAME/KEY: other

(B) LOCATION: complement(115..313)

(C) IDENTIFICATION METHOD: blastn
(D) OTHEE INFORMATION: identity 98

region 1..199 id H19659

est

(ix) FEATURE:

(A) NAME (HEY: other

WO 99/06552

(B) LOCATION: complement(2..102)

(C) IDENTIFICATION METHOD: blastn

(D) OTHER INFORMATION: identity 97

region 212..312 id H19659

est

#### (ix) FEATURE:

(A) NAME/KEY: other

(B) LOCATION: complement(115..313)

(C) IDENTIFICATION METHOD: blastn

(D) OTHER INFORMATION: identity 97

region 1..199

id R72881

est

#### (ix) FEATURE:

(A) NAME/KEY: other

(B) LOCATION: complement(115..290)

(C) IDENTIFICATION METHOD: blastn

(D) OTHER INFORMATION: identity 98

region 1..176

id H50517

est

#### (ix) FEATURE:

(A) NAME/KEY: other

(B) LOCATION: complement (44..102)

(C) IDENTIFICATION METHOD: blastn

(D) OTHER INFORMATION: identity 100

region 189..247

id H50517

est

#### (ix) FEATURE:

(A) NAME/KEY: other

(B) LOCATION: complement(115..302)

(C) IDENTIFICATION METHOD: blastn

(D) OTHER INFORMATION: identity 96

region 36..223

id H41556

est

## (ix) FEATURE:

(A) NAME/KEY: other

(B) LOCATION: complement(115..313)

(C) IDENTIFICATION METHOD: blastn

(D) OTHER INFORMATION: identity 95

region 2..200

id R71794

est

# (ix) FEATURE:

(A) NAME/KEY: other

(B) LOCATION: complement(44..102)

(C) IDENTIFICATION METHOD: blastn

(D) OTHER INFORMATION: identity 96

region 213..271

id R71794

est

WO 99/065	552	251	PC	T/IB98/0
(ix)	FEATURE:  (A) NAME/KEY: sig_pe (B) LOCATION: 2292 (C) IDENTIFICATION M (D) @THER INFORMATION	ptide 76 ETHOD: Von N: score 4	Heijne matrix .2 SLSYCGVSWG/RI	
(xi)	SEQUENCE DESCRIPTION:	SEQ ID NO:	244:	
ACATTTCTGC	TCAGATTCCC GCCATCTCCA	TTGCATTCAT	GTACTACCCT CAGTCTACA	C 60
TCACAATCAT	CTTCTCCCAA GACTGCTCCC	TTTTGTTTTG	TGTTTTTTTG AGGGGAATT	A 120
AGGAAAAATA	AGTGGGGGCA GGTTTGGAGA	GCTGCTTCCA	GTGGATAGTT GATGAGAATO	2 180
	GAAGGCACCC TTGACTGTYG		Met Gly Trp -15	237
GAG GTG GTC Glu Val Val	G TCC CTT TCA TAC TGT G . Ser Leu Ser Tyr Cys G -10	GT GTC TCT ly Val Ser -5	TGG GGA AGG ATC TCC Trp Gly Arg Ile Ser 1	285
CCG AAT CTC Pro Asn Leu 5	: AAT AAA CCA GTG AAC A : Asn Lys Pro Val Asn A 10	GG rg		312
(i) S (ii) t (vi) (	EQUENCE CHARACTERISTICS  (A) LENGTH: 252 base F  (B) TYPE: NUCLEIC ACID  (C) STRANDEDNESS: DOUB  (D) TOPOLOGY: LINEAR  MOLECULE TYPE: CDNA  PRIGINAL SOURCE:  (A) ORGANISM: Homo Sap  (F) TISSUE TYPE: Brain  TEATURE:  (A) NAME/KEY: other  (B) LOCATION: 41210  (C) IDENTIFICATION MET.  (D) OTHER INFORMATION:	S: pairs ) ULE iens	98	
(iv) E	TATUS.			

(A) MAME/KEY: sig\_peptide (B) LOCATION: 37..132

(C) IDENTIFICATION METHOD: Von Heijne matrix (D) OTHER INFORMATION: score 4.2 seq CWELFCLEHGIQA/DG

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 245:

WO 99/06552

AAAC	GCTGA	AGA (	GKGC	CGCGC	GG CC	SAGG	ACAGO	GGC	CASR		GAA Glu -30		54
	CAC His -25												102
	TTC Phe												150
	GCT Ala												198
	ACT Thr												246
	AAA Lys 40												252

## (2) INFORMATION FOR SEQ ID NO: 246:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 172 base pairs

(B) TYPE: NUCLEIC ACID

(C) STRANDEDNESS: DOUBLE

(D) TOPOLOGY: LINEAR

(ii) MOLECULE TYPE: CDNA

(vi) ORIGINAL SOURCE:

(A) ORGANISM: Homo Sapiens

(F) TISSUE TYPE: Brain

(ix) FEATURE:

(A) NAME/KEY: other

(B) LOCATION: 82..168

(C) IDENTIFICATION METHOD: blastn

(D) OTHER INFORMATION: identity 96

region 107..193 id AA088577

est

(ix) FEATURE:

(A) NAME/KEY: other

(B) LOCATION: 31..71

(C) IDENTIFICATION METHOD: blastn

(D) OTHER INFORMATION: identity 92

region 53..93 id AA088577

est

WO 99/06552 253 (A) NAME/KEY: other (B) LOCATION: 31..168 (C) IDENTIFICATION METHOD: blastn (D) OTHER INFORMATION: identity 97 region 24..161 id R16448 est (ix) FEATURE: (A) NAME/KEY: other (B) LOCATION: 53..168 (C) IDENTIFICATION METHOD: blastn (D) OTHER INFORMATION: identity 99 region 23..138 id AA094092 est (ix) FEATURE: (A) NAME/KEY: other (B) LOCATION: 31..163 (C) IDENTIFICATION METHOD: blastn (D) OTHER INFORMATION: identity 96 region 24..156 id R18030 est (ix) FEATURE: (A) NAME/KEY: other (B) LOCATION: 60..168 (C) IDENTIFICATION METHOD: blastn (D) OTHER INFORMATION: identity 97 region 43..151 id W00599 (ix) FEATURE: (A) NAME/KEY: other (B) LOCATION: 29..70 (C) IDENTIFICATION METHOD: blastn (D) OTHER INFORMATION: identity 95 region 13..54 id W00599 est (ix) FEATURE: (A) NAME/KEY: sig\_peptide (B) LOCATION: 35..109 (C) IDENTIFICATION METHOD: Von Heijne matrix (D) OTHER INFORMATION: score 4.2 seq LDLLRGLPRVSLA/NL (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 246: AAGGGCGCCC TTCAAAGTTC TTGGATCTGC GGGT ATG GCC GGT CCC TTG CAG GGC Met Ala Gly Pro Leu Gln Gly -25 GGT GGG GCC CGG GGC CTG GAC CTA CTC CGG GGC CTG CCG CGT GTG AGC

Gly Gly Ala Arg Ala Leu Asp Leu Leu Arg Gly Leu Pro Arg Val Ser

-10

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CTG GCC AAC TTA AAG CCG AAT CCC GGC TCC AAG AAA CCG GAG AGA AGA
Leu Ala Asn Leu Lys Pro Asn Pro Gly Ser Lys Lys Pro Glu Arg Arg

1 5 10

CCA AGA GGT CGG AGA AGG TGG Pro Arg Gly Arg Arg Arg Trp 15 20 172

## (2) INFORMATION FOR SEQ ID NO: 247:

## (i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 359 base pairs
- (B) TYPE: NUCLEIC ACID
- (C) STRANDEDNESS: DOUBLE
- (D) TOPOLOGY: LINEAR
- (ii) MOLECULE TYPE: CDNA
- (vi) ORIGINAL SOURCE:
  - (A) ORGANISM: Homo Sapiens
  - (F) TISSUE TYPE: Brain
- (ix) FEATURE:
  - (A) NAME/KEY: other
  - (B) LOCATION: 52..360
  - (C) IDENTIFICATION METHOD: blastn
  - (D) OTHER INFORMATION: identity 98 region 1..309

id HSC1ED081

est

## (ix) FEATURE:

- (A) NAME/KEY: other
- (B) LOCATION: 171..316
- (C) IDENTIFICATION METHOD: blastn
- (D) OTHER INFORMATION: identity 98

region 146..291 id AA143136

est

#### (ix) FEATURE:

- (A) NAME/KEY: other
- (B) LOCATION: 31..165
- (C) IDENTIFICATION METHOD: blastn
- (D) OTHER INFORMATION: identity 97

region 6..140 id AA143136

est

## (ix) FEATURE:

- (A) NAME/KEY: other
- (B) LOCATION: 310..341
- (C) IDENTIFICATION METHOD: blastn
- (D) OTHER INFORMATION: identity 96 region 286..317 id AA143136

			( <i>E</i> ( C	3) LC 3) IE	AME/K DCATI DENTI THER	ON:	176.	.282 1 MET	HOD: id re	lenti gion N75	ty 9	9 .183				
		(ix)	(B (C	) NA ) LO ) ID	: ME/K CATIO ENTII HER :	ON: FICA	102. TION	.165 MET	id re	enti gion N75	ty 9	9 66				
		(ix)	(C)	LOC I DE	: ME/KE CATIC CNTIF HER I	N: 1 ICAT	.56 'ION	230 METE	IOD:	re 4	. 2	ine m				
ATI					DES				Q ID	NO:	247	':				
CCC	TCCA	CTT TT	ccac	.01.00		CMGI	CCGC	T CC	GTCC	GCCC	TTA	GACC	TGT	TGCC	CAGCAT	60
CTC	CACA	Cmm		GWAC	AG T	CTCT	ATTA	G AG	CGCG	TGTA	TAG	AGGC	AGA	KAGG	AGTGA.ª	120
										-25	Pro	Ala	Gly		Pro -20	173
				-15			2	ma	-10	ser	хаа	Leu	Ala	ATG Met -5	Cys	221
GCA Ala	GGG Gly	GCA Ala	GAA Glu 1	GTG Val	GTG Val	CAC His	AGG Arg 5	TAC Tyr	TAC Tyr	CGA Arg	CCG Pro	GAC Asp 10	CTG Leu	ACA Thr	ATA Ile	269
CCT Pro	GAA Glu 15	ATT Ile	CCA Pro	CCA Pro	AAG Lys	CGT Arg 20	GGA Gly	GAA Glu	CTC Leu	AAA Lys	ACG Thr 25	GAG Glu	CTT Leu	TTG Leu	GGA Gly	317
CTG Leu 30	AAA Lys	GAA Glu	AGA Arg	AAA Lys	CAC His 35	AAA Lys	CCT Pro	CAA Gln	GTT Val	TCT Ser 40	CAA Gln	CAG Gln	GAG Glu			359
(2)	INFO	RMAT	'ION	FOR	SEQ	ID N	10: 2	248:								

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 284 base pairs
(B) TYPE: NUCLEIC ACID
(C) STRANDEDNESS: DOUBLE
(D) TOPOLOGY: LINEAR

```
(ii) MOLECULE TYPE: CDNA
```

## (vi) ORIGINAL SOURCE:

(A) ORGANISM: Homo Sapiens

(F) TISSUE TYPE: Brain

#### (ix) FEATURE:

(A) NAME/KEY: other

(B) LOCATION: 10..280

(C) IDENTIFICATION METHOD: blastn

(D) OTHER INFORMATION: identity 98

region 17..287

id AA082102

est

#### (ix) FEATURE:

(A) NAME/KEY: other

(B) LOCATION: 72..224

(C) IDENTIFICATION METHOD: blastn

(D) OTHER INFORMATION: identity 98

region 30..182

id R10417

est

#### (ix) FEATURE:

(A) NAME/KEY: other

(B) LOCATION: 221..280

(C) IDENTIFICATION METHOD: blastn

(D) OTHER INFORMATION: identity 100

region 180..239

id R10417

est

#### (ix) FEATURE:

(A) NAME/KEY: other

(B) LOCATION: 47..280

(C) IDENTIFICATION METHOD: blastn

(D) OTHER INFORMATION: identity 99

region 2..235

id W73318

est

## (ix) FEATURE:

(A) NAME/KEY: other

(B) LOCATION: 42..224

(C) IDENTIFICATION METHOD: blastn

(D) OTHER INFORMATION: identity 97

region 1..183

id R08733

est

## (ix) FEATURE:

(A) NAME/KEY: other

(B) LOCATION: 237..269

(C) IDENTIFICATION METHOD: blastn

(D) OTHER INFORMATION: identity 93

region 198..230

id R08733

257

	(ix) FEATURE:  (A) NAME/KEY: sig_peptide  (B) LOCATION: 39110  (C) IDENTIFICATION METHOD: Von Heijne matrix  (D) OTHER INFORMATION: score 4.2  seq SLPALALSLRASP/RX  (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 248:															
	(×	i) S	SEQUE	NCE	DESC	RIPT	`ION:	SEC	) ID	NO:	248:					
AAGI	Met Ala Val Gln Cys Val -20															56
														AGG Arg		104
														GGC Gly		152
														CCT Pro		200
														GAA Glu 45		248
					GAA Glu											284
(2)	INF	ORMA	поіт	FOR	SEQ	ID	NO:	249:								
	(	i) S	(A) (B) (C)	LENG TYP STR	CHAR GTH: E: NI ANDE OLOG	307 UCLE DNES	base IC AG S: DG	e pa. CID CUBL:								

- (ii) MOLECULE TYPE: CDNA
- (vi) ORIGINAL SOURCE:
  - (A) ORGANISM: Homo Sapiens
  - (F) TISSUE TYPE: Brain
- (1K) FEATURE:
  - (A) NAME/KEY: other
  - (B) LOCATION: complement(34..74)
  - (C) IDENTIFICATION METHOD: blastn
  - (D) OTHER INFORMATION: identity 92 region 271..311 id T05270

est

(ix) FEATURE:

(A) NAME/KEY: sig\_peptide

WO 99/06552	258 PC1/II	398/012
(C)	LOCATION: 182292 IDENTIFICATION METHOD: Von Heijne matrix OTHER INFORMATION: score 4.2 seq RLMHHYLSTPTSA/RP	
(xi) SEQUE	NCE DESCRIPTION: SEQ ID NO: 249:	
AAAGGCTGCC CTGTG	GGCACC ACAATCTAAG CTCAGGGCAT AAAACCCCTT GTGGCTTTGA	60
TGGAATCCAG GGCTC	CAGACC ATAAAACCCC TCGTGGCCTT TTGAATGTGC ACCGACTTGC	120
TGGCTCCTTG CTTCT	TTGCTC TCCCAGAATC GTAAATTGAT TGTATCTTGA GTTGGAAGAA	180
	TT ATC TCA CGT AGC AGA GCA TGT TCC ATG TAC TTC AAA Le Ile Ser Arg Ser Arg Ala Cys Ser Met Tyr Phe Lys -30 -25	229
	CCG TCA CAG CTA CGC TTG ATG CAC CAC TAC CTT TCT Pro Ser Gln Leu Arg Leu Met His His Tyr Leu Ser -15 -10	277
	GCA CGT CCT CAC CTG Ala Arg Pro His His Leu 1 5	307
(i) SEQUENT (A) (B) (C) (D)	FOR SEQ ID NO: 250:  NCE CHARACTERISTICS:  LENGTH: 212 base pairs  TYPE: NUCLEIC ACID  STRANDEDNESS: DOUBLE  TOPOLOGY: LINEAR  CULE TYPE: CDNA  INAL SOURCE:	
(A)	ORGANISM: Homo Sapiens TISSUE TYPE: Brain	
(B) (C)	URE: NAME/KEY: other LOCATION: complement(1209) IDENTIFICATION METHOD: blastn OTHER INFORMATION: identity 99 region 125333 id H40205 est	
(ix) FEAT	CURE:	

- (A) NAME/KEY: other

- (B) LOCATION: complement(80..209)
  (C) IDENTIFICATION METHOD: blastn
  (D) OTHER INFORMATION: identity 96
  region 131..260 id H03462

est

'im) FEATURE:

259 (A) NAME/KEY: other (B) LOCATION: complement(52..90) (C) IDENTIFICATION METHOD: blastn (D) OTHER INFORMATION: identity 97 region 251..289 id H03462 est (ix) FEATURE: (A) NAME/KEY: other (B) LOCATION: complement(17..54) (C) IDENTIFICATION METHOD: blastn (D) OTHER INFORMATION: identity 97 region 288..325 id H03462 est (ix) FEATURE: (A) NAME/KEY: other (B) LOCATION: complement(17..209) (C) IDENTIFICATION METHOD: blastn (D) OTHER INFORMATION: identity 95

## (ix) FEATURE:

- (A) NAME/KEY: other
- (B) LOCATION: complement(128..209)
- (C) IDENTIFICATION METHOD: blastn
- (D) OTHER INFORMATION: identity 98

region 143..224

region 130..322 id R05443 est

id T52770

est

#### (ix) FEATURE:

- (A) NAME/KEY: other
- (B) LOCATION: complement(80..128)
- (C) IDENTIFICATION METHOD: blastn
- (D) OTHER INFORMATION: identity 100

region 225..273 id T52770

est

#### (ix) FEATURE:

- (A) NAME/KEY: other
- (B) LOCATION: complement(43..74)
- (C) IDENTIFICATION METHOD: blastn
- (D) OTHER INFORMATION: identity 96

region 281..312

id T52770

est

## (ix) FEATURE:

- (A) NAME/KEY: other
- (B) LOCATION: complement(57..209)
- (C) IDENTIFICATION METHOD: blastn

(D) OTHER INFORMATION: identity 98

region 143..295

id AA037595

(ix) FEATURE:  (A) NAME/KEY: sig_peptide  (B) LOCATION: 108155  (C) IDENTIFICATION METHOD: Von Heijne matrix  (D) OTHER INFORMATION: score 4.1  seq LLPATSLAGPVLS/TL  (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 250:														
(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 250:														
ACTTCTTGTG GACTCACCAA GAGAAACAAA AGGAAGCCTG CACCATTGTA GCCCTGAACT	60													
CTTTTCTGGG CACCTGAATC CCAGGAACCC TCAATGAGGT CTTCAAG ATG AAG AGA Met Lys Arg -15	1,16													
CTG CTG CCA GCT ACC AGC CTG GCT GGC CCT GTC CTG TCC ACC CTC ATT Leu Leu Pro Ala Thr Ser Leu Ala Gly Pro Val Leu Ser Thr Leu Ile -10 -5 1	164													
GCC CCA ACT CCC ATG TTG TTT TGT GAA GAT AAA AGC TGG GAT CCT GGG Ala Pro Thr Pro Met Leu Phe Cys Glu Asp Lys Ser Trp Asp Pro Gly 5	212													
(2) INFORMATION FOR SEQ ID NO: 251:														
<ul> <li>(i) SEQUENCE CHARACTERISTICS:</li> <li>(A) LENGTH: 357 base pairs</li> <li>(B) TYPE: NUCLEIC ACID</li> <li>(C) STRANDEDNESS: DOUBLE</li> <li>(D) TOPOLOGY: LINEAR</li> </ul>														
(ii) MOLECULE TYPE: CDNA														
<pre>(vi) ORIGINAL SOURCE:     (A) ORGANISM: Homo Sapiens     (F) TISSUE TYPE: Brain</pre>														
(ix) FEATURE:  (A) NAME/KEY: other  (B) LOCATION: 108308  (C) IDENTIFICATION METHOD: blastn  (D) OTHER INFORMATION: identity 95  region 116316  id HSC2TH021  est														
<pre>(ix) FEATURE:     (A) NAME/KEY: other     (B) LOCATION: 1699     (C) IDENTIFICATION METHOD: blastn     (D) OTHER INFORMATION: identity 97</pre>														

est

(ix) FEATURE:

(A) NAME/KEY: other

WO 99/06552 PCT/IB98/01236

***	<i>J</i> 99/0	شدده							261						101/	1270.01
			(€)	IDEN	TIFI	: 30 CATI FORM	ON M	ETHO N:	iden regi	last tity on 7 5452	92 21	34				
	(i	ж) F	(A) (B) (C)	NAME LOCA IDEN	TION TIFI	: ot : 11 CATI FORM	93 ON M	ETHO	ıden regi	last tity on 2 5968	98 32	56				
	(i	.×) F	(A) (B) (C)	NAME LOCA IDEN	TION TIFI	: si I: 64 CATI IFORM	27 ON M	3 ETHC	D: V	e 4	-	e ma YDVF				
	( x	i) S	EQUE	ENCE	DESC	CRIPI	'ION:	SEC	OID	NO:	251:					
AAC1	rgtco	CGG C	GCT	GCGG	GG CI	TTGCT	TCCC	G GC	STCAT	GGC	TCAA	\AGG(	GCC 1	TCCC	CGAATC	60
CTT						AAT Asn -65										108
GGG Gly -55	AGG Arg	CTG Leu	ACT Thr	CCT Pro	GAG Glu -50	TTC Phe	TCA Ser	CAA Gln	CGC Arg	TTG Leu -45	ACC Thr	AAT Asn	AAG Lys	ATT Ile	CGG Arg -40	156
						GAG Glu										204
				Tyr		GGC Gly										252
						GGG Gly										300
	Tyr					CTG Leu										348
	CAA Gln															357

(2) INFORMATION FOR SEQ ID NO: 252:

(1) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 414 base pairs

- (B) TYPE: NUCLEIC ACID(C) STRANDEDNESS: DOUBLE
- (D) TOPOLOGY: LINEAR
- (ii) MOLECULE TYPE: CDNA
- (vi) ORIGINAL SOURCE:
  - (A) ORGANISM: Homo Sapiens
  - (F) TISSUE TYPE: Brain
- (ix) FEATURE:
  - (A) NAME/KEY: other
  - (B) LOCATION: 11..238
  - (C) IDENTIFICATION METHOD: blastn
  - (D) OTHER INFORMATION: identity 100 region 1..228 id R26618

- (ix) FEATURE:
  - (A) NAME/KEY: other
  - (B) LOCATION: 283..397
  - (C) IDENTIFICATION METHOD: blastn
  - (D) OTHER INFORMATION: identity 98 region 96..210 id HUM528H09B

est

est

- (ix) FEATURE:
  - (A) NAME/KEY: other
  - (B) LOCATION: 202..282
  - (C) IDENTIFICATION METHOD: blastn
  - (D) OTHER INFORMATION: identity 98

region 16..96 id HUM528H09B

est

- (ix) FEATURE:
  - (A) NAME/KEY: other
  - (B) LOCATION: 283..411
  - (C) IDENTIFICATION METHOD: blastn
  - (D) OTHER INFORMATION: identity 96 region 110..238

id C18739

est

- (ix) FEATURE:
  - (A) NAME/KEY: other
  - (B) LOCATION: 202..282
  - (C) IDENTIFICATION METHOD: blastn
  - (D) OTHER INFORMATION: identity 98

region 30..110

id C18739

- (ix) FEATURE:
  - (A) NAME/KEY: other
  - (B) LOCATION: 235..411
  - (C) IDENTIFICATION METHOD: blastn
  - (D) OTHER INFORMATION: identity 97 region 1...177

id E17985 est

(ix) FEATURE:	E :
---------------	-----

- (A) MAME/KEY: other
- (B) LOCATION: complement(2..70)
- (C) IDENTIFICATION METHOD: blastn
- (D) OTHER INFORMATION: identity 97

region 9..77 id R40947 est

#### (ix) FEATURE:

- (A) NAME/KEY: sig\_peptide
- (B) LOCATION: 274..336
- (C) IDENTIFICATION METHOD: Von Heijne matrix
- (D) OTHER INFORMATION: score 3.9

seq AWLAQGSSSAGWG/LE

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 252:

ATCAATTTK TGAATAGTTT CCATTTCAAA TATCTTGTTC TACTTGGTTC ATAAAATAGT 60

GGTTTTCAAA CTGTAGAGCT CTGGACTTCT CACTTCTAGG GCAGAGGGAG CCTGAACAAG 120

TGAGGCTCTG GGTTCCCCAT TCCTAATTAA ACCAATGGAA AGAAGGGGTC TAATAACAAA 180

CTACAGCAAC ACATTTTCA TTTCAGCTTC ACTGCTGTAT CTCCCAGTCT AACCCTAGCA 240

TCCAGAAAGTG GCACAAAACC CCTCTGCTGG CTC ATG TGT GCA ACT GAG ACT GTC 294

Met Cys Ala Thr Glu Thr Val -20 -15

AGA GCA TGG CTA GCT CAG GGG TCC AGC TCT GCA GGG TGG GGG CTA GAG

Arg Ala Trp Leu Ala Gln Gly Ser Ser Ser Ala Gly Trp Gly Leu Glu

-10

-5

AGG AAG CAG GGA GTA TCT GCA CAC AGG ATG CCC GCG CTC AGG TGG TTG 390
Arg Lys Gln Gly Val Ser Ala His Arg Met Pro Ala Leu Arg Trp Leu

5 10

CAG AAG TCA GTG CCA GGA BCC ATG 414
Gln Lys Ser Val Pro Gly Xaa Met 20 25

#### (2) INFORMATION FOR SEQ ID NO: 253:

- (i) SEQUENCE CHARACTERISTICS:
  - (A) LENGTH: 189 base pairs
  - (B) TYPE: NUCLEIC ACID
  - (C) STRANDEDNESS: DOUBLE
  - (D) TOPOLOGY: LINEAR
- (ii) MOLECULE TYPE: CDNA
- (vi) ORIGINAL SOURCE:
  - (A) ORGANISM: Homo Sapiens
  - (F) TISSUE TYPE: Brain

```
(ix) FEATURE:
```

- (A) NAME/KEY: other
- (B) LOCATION: 124..153
- (C) IDENTIFICATION METHOD: blastn
- (D) OTHER INFORMATION: identity 90

region 25..54 id N91869

est

(ix) FEATURE:

- (A) NAME/KEY: other
- (B) LOCATION: 124..153
- (C) IDENTIFICATION METHOD: blastn
- (D) OTHER INFORMATION: identity 90

region 5..34 id H53427

est

(ix) FEATURE:

- (A) NAME/KEY: other
- (B) LOCATION: 124..153
- (C) IDENTIFICATION METHOD: blastn
- (D) OTHER INFORMATION: identity 90

region 19..48

id H88369

est

(ix) FEATURE:

- (A) NAME/KEY: other
- (B) LOCATION: 124..153
- (C) IDENTIFICATION METHOD: blastn
- (D) OTHER INFORMATION: identity 90

region 26..55

id T79771

est

(ix) FEATURE:

- (A) NAME/KEY: other
- (B) LOCATION: 124..153
- (C) IDENTIFICATION METHOD: blastn
- (D) OTHER INFORMATION: identity 90

region 29..58

id H41152

est

(ix) FEATURE:

- (A) NAME/KEY: sig\_peptide
- (B) LOCATION: 46..183
- (C) IDENTIFICATION METHOD: Von Heijne matrix
- (D) OTHER INFORMATION: score 3.9

seq AAAFCLKXXGANT/HP

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 253:

AGAATTTCTC CCACTCTTCG AGCCTACAGC AGACATGTTA GGAGA ATG CTG CTT

Met Leu Leu Leu

57

-45

GCA ACA CAC CCA GAG ACG GTG GGG CAG GTG ACA CTG CGT GTG TRC CCG

265 Ala Thr His Pro Glu Thr Val Gly Gln Val Thr Leu Ard Val Xaa Pro -35 GTG TCT CTG GAA GTG TCT ATA CAG ATG TGT GCT GCT GCT GCT GCT Val Ser Leu Glu Val Ser Ile Gln Met Cys Ala Ala Ala Ala Ala Ala 153 -20 TTC TGC CTT AAA ATK WCT GGA GCC AAC ACC CAC CCA Phe Cys Leu Lys Xaa Xaa Gly Ala Asn Thr His Pro 189 - 5

## (2) INFORMATION FOR SEQ ID NO: 254:

- (i) SEQUENCE CHARACTERISTICS:
  - (A) LENGTH: 300 base pairs
  - (B) TYPE: NUCLEIC ACID
  - (C) STRANDEDNESS: DOUBLE
  - (D) TOPOLOGY: LINEAR
- (ii) MOLECULE TYPE: CDNA
- (vi) ORIGINAL SOURCE:
  - (A) ORGANISM: Homo Sapiens
  - (F) TISSUE TYPE: Brain
- (ix) FEATURE:
  - (A) NAME/KEY: other
  - (B) LOCATION: 149..232
  - (C) IDENTIFICATION METHOD: blastn

(D) OTHER INFORMATION: identity 96 region 91..174 id AA081517

- (ix) FEATURE:
  - (A) NAME/KEY: other
  - (B) LOCATION: 224..297
  - (C) IDENTIFICATION METHOD: blastn
  - (D) OTHER INFORMATION: identity 97

region 165..238

id AA081517

- (ix) FEATURE:
  - (A) NAME/KEY: other
  - (B) LOCATION: 90..141
  - (C) IDENTIFICATION METHOD: blastn
  - (D) OTHER INFORMATION: identity 98

region 34..85 id AA081517

- (ix) FEATURE:
  - (A) NAME/KEY: other
  - (B) LOCATION: 76..141
  - (C) IDENTIFICATION METHOD: blastn
  - (C) OTHER INFORMATION: identity 93 region 20..85 id N53273

	(i	.x) E	(A) (B) (C)	JRE: NAME LOCA IDEN OTHE	TION	: 14 CATI	91 ON M	ЕТНС	iden regi	last tity on 9	97 911	.35				
	(i	×) F	(A) (B) (C)	IRE: NAME LOCA IDEN OTHE	TION	: cc	mple ON M	ETHO		last tity on 1	n 100 72					
	·	x) E	(A) (B) (C) (D)	IRE: NAME LOCA IDEN OTHE	TION TIFI R IN	: 43 CATI	ON M	4 ETHO N:	D: V scor seq	e 3. GLGG	9 AQLQ	)GGAX	itrix G/RG			
AGTO	CTCTC	GG C	GCGG	GCCAT	rg Ti	rggac	GSTO	CGC	GCC	CGAG				GCG #		54
TCA Ser -60	GCA Ala	ACC Thr	CCA Pro	GCG Ala	CCS Pro -55	ASC Xaa	RGA Xaa	AGT Ser	CAG Gln	CGG Arg -50	TGC Cys	GGG Gly	GCA Ala	GAT Asp	GCT Ala -45	102
GGA Gly	AGT Ser	GCA Ala	GCC Ala	AGG Arg -40	ATT Ile	GTA Val	TTT Phe	CGG Arg	TGG Trp -35	GGC Gly	CGC Arg	GGC Gly	CGT Arg	CGC Arg -30	GGA Gly	150
GCC Ala	AGA Arg	TCA Ser	CCT Pro -25	GAG Glu	GGA Gly	AGC Ser	GGG Gly	CAT His -20	CAC His	GGC Gly	CGT Arg	GCT Ala	AAC Asn -15	AGT Ser	GGA Gly	198
CTC Leu	GGA Gly	GGA Gly -10	GCC Ala	CAG Gln	CTT Leu	CAA Gln	GGC Gly -5	GGG Gly	GCC Ala	TRG Xaa	GGT Gly	CGA Arg 1	GGA Gly	TCT Ser	ATG Met	246
GCG Ala 5	CCT Pro	CTT Leu	CGT Arg	GCC Ala	AGC Ser 10	GCT Ala	GGA Gly	CAA Gln	ACC Thr	CGA Arg 15	GAC Asp	GGA Gly	CCT Pro	ACT Thr	CAG Gln 20	294
	GGG Gly															300

- (2) INFORMATION FOR SEQ ID NO: 255:
  - (i) SEQUENCE CHARACTERISTICS:

267 (A) LENGTH: 151 base pairs (B) TYPE: NUCLEIC ACID (C) STRANDEDNESS: DOUBLE (D) TOPOLOGY: LINEAR (ii) MOLECULE TYPE: CDNA (vi) ORIGINAL SOURCE: (A) ORGANISM: Homo Sapiens (F) TISSUE TYPE: Brain (ix) FEATURE: (A) NAME/KEY: other (B) LOCATION: 13..150 (C) IDENTIFICATION METHOD: blastn (D) OTHER INFORMATION: identity 100 region 1..138 id T36282 est (ix) FEATURE: (A) NAME/KEY: other (B) LOCATION: 46..150 (C) IDENTIFICATION METHOD: blastn (D) OTHER INFORMATION: identity 99 region 1..105 id T08090 (ix) FEATURE: (A) NAME/KEY: other (B) LOCATION: 46..150 (C) IDENTIFICATION METHOD: blastn (D) OTHER INFORMATION: identity 99 region 1..105 id T08091 est (ix) FEATURE: (A) NAME/KEY: other (B) LOCATION: 72..150 (C) IDENTIFICATION METHOD: blastn (D) OTHER INFORMATION: identity 98 region 1..79 id H56620 (ix) FEATURE: (A) NAME/KEY: other (B) LOCATION: 80..150 (C) IDENTIFICATION METHOD: blastn (D) OTHER INFORMATION: identity 100 region 1..71 id AA027983 AST (ix) FEATURE: (A) NAME/KEY: sig\_peptide (B) LOCATION: 2..52 (C) IDENTIFICATION METHOD: Von Heijne matrix 3) OTHER INFORMATION: score 3.9

## seq PLAGLAAAALGRA/PP

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 255:

A ATG CTG CGG CGC CCG CTG GCC GGG CTG GCT GCG GCC CTG GGC CGG

Met Leu Arg Arg Pro Leu Ala Gly Leu Ala Ala Ala Leu Gly Arg

-15

-10

-5

GCC CCA CCG GAC GGC TTG CTC TGC TCT TTA CCT GGG GTT GCT GTC GAG

Ala Pro Pro Asp Gly Leu Leu Cys Ser Leu Pro Gly Val Ala Val Glu

1 5 10 15

GAC CCT GTG CAA GAC TCG GCC GGT TTT TCT TCC CTG ATG GAC AGA
Asp Pro Val Gln Asp Ser Ala Gly Phe Ser Phe Ser Leu Met Asp Arg
20 25 30

CCC AAG
Pro Lys

## (2) INFORMATION FOR SEQ ID NO: 256:

- (i) SEQUENCE CHARACTERISTICS:
  - (A) LENGTH: 217 base pairs
    - (B) TYPE: NUCLEIC ACID
    - (C) STRANDEDNESS: DOUBLE
    - (D) TOPOLOGY: LINEAR
- (ii) MOLECULE TYPE: CDNA
- (vi) ORIGINAL SOURCE:
  - (A) ORGANISM: Homo Sapiens
  - (F) TISSUE TYPE: Brain
- (ix) FEATURE:
  - (A) NAME/KEY: other
    - (B) LOCATION: 3..214
    - (C) IDENTIFICATION METHOD: blastn
    - (D) OTHER INFORMATION: identity 99 region 14..225 id H08058 est

(ix) FEATURE:

- (A) NAME/KEY: other
- (B) LOCATION: 2..91
- (C) IDENTIFICATION METHOD: blastn
- (D) OTHER INFORMATION: identity 100 region 10..99 id R11727 est
- (ix) FEATURE:
  - (A) NAME/KEY: sig\_peptide
  - (B) LOCATION: 59..109
  - (C) IDENTIFICATION METHOD: Von Heijne matrix
  - (D) OTHER INFORMATION: score 3.8 seq GFVAALVAGGVAG/VS

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 256:

AGACGTGATC CGCTTCTGCT CCGGCTTGGA TTGTAGCCTT GACGAGGTCT GAGCGACC 58 ATG GAC CGG CCG GGG TTC GTG GCA GCG CTG GTG GCT GGT GGG GTA GCA Met Asp Arg Pro Gly Phe Val Ala Ala Leu Val Ala Gly Gly Val Ala 106 -10 GGT GTT TCT GTT GAC TTG ATA TTA TTT CCT CTG GAT ACC ATT AAA ACC Gly Val Ser Val Asp Leu Ile Leu Phe Pro Leu Asp Thr Ile Lys Thr 154 AGG CTG CAG AGT CCC CAA GGA TTT AGT AAG GCT GGT GGT TTT CAT GGA Arg Leu Gln Ser Pro Gln Gly Phe Ser Lys Ala Gly Gly Phe His Gly 25 ATA TAT GCT AGC TGG Ile Tyr Ala Ser Trp 217 35

- (2) INFORMATION FOR SEQ ID NO: 257:
  - (i) SEQUENCE CHARACTERISTICS:
    - (A) LENGTH: 158 base pairs
    - (B) TYPE: NUCLEIC ACID
    - (C) STRANDEDNESS: DOUBLE
    - (D) TOPOLOGY: LINEAR
  - (ii) MOLECULE TYPE: CDNA
  - (vi) ORIGINAL SOURCE:
    - (A) ORGANISM: Homo Sapiens
    - (F) TISSUE TYPE: Brain
  - (ix) FEATURE:
    - (A) NAME/KEY: other
    - (B) LOCATION: 39..155
    - (C) IDENTIFICATION METHOD: blastn
    - (D) OTHER INFORMATION: identity 98 region 1..117 id C01598 est
  - (ix) FEATURE:
    - (A) NAME/KEY: sig\_peptide
    - (B) LOCATION: 9..71
    - (C) IDENTIFICATION METHOD: Von Heijne matrix
    - (D) OTHER INFORMATION: score 3.8

seq SMDLLTLLFQRRS/HQ

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 257:

AATCAAGT ATG ATT GTT TGG TTT GAG GGT ATT TCC ATG GAT CTC CTT ACA 50

Met Ile Val Trp Phe Glu Gly Ile Ser Met Asp Leu Leu Thr
-20 -10

CTG CTA TITC CAG AGG AGA AGC CAG CAG GTC ACT CAA CTC TTA GTA TCA

PCT/IB98/01236 WO 99/06552 270

Leu Leu Phe Gln Arg Arg Ser His Gln Val Thr Gln Leu Leu Val Ser

TCT ACT GGA AAC TGG CTA AGA CAG TAT TTA TGT GCT TCT CTC ACA ATA Ser Thr Gly Asn Trp Leu Arg Gln Tyr Leu Cys Ala Ser Leu Thr Ile 15 20

GCA GGA AGA AGG 158 Ala Gly Arg Arg

#### (2) INFORMATION FOR SEQ ID NO: 258:

- (i) SEQUENCE CHARACTERISTICS:
  - (A) LENGTH: 292 base pairs
  - (B) TYPE: NUCLEIC ACID
  - (C) STRANDEDNESS: DOUBLE
  - (D) TOPOLOGY: LINEAR
- (ii) MOLECULE TYPE: CDNA
- (vi) ORIGINAL SOURCE:
  - (A) ORGANISM: Homo Sapiens
  - (F) TISSUE TYPE: Brain
- (ix) FEATURE:

. .

- (A) NAME/KEY: other
- (B) LOCATION: complement(192..269)
- (C) IDENTIFICATION METHOD: blastn
- (D) OTHER INFORMATION: identity 92 region 354..431 id N70088
- (ix) FEATURE:
  - (A) NAME/KEY: other
  - (3) LOCATION: complement(222..262)
  - (C) IDENTIFICATION METHOD: blastn
  - (D) OTHER INFORMATION: identity 95

region 399..439 id H30254

est

est

- (ix) FEATURE:
  - (A) NAME/KEY: sig\_peptide
  - (3) LOCATION: 143..202
  - (C) IDENTIFICATION METHOD: Von Heijne matrix
  - (D) OTHER INFORMATION: score 3.8

seq ALDALMFPARRRA/AV

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 258:

AAGCGGCTGT CCTCCCTCGC TTTTGGAGCT CCGACCTCAG CTTCGCCTGC GAGCTGGGTT 60

GTGTAAAGGC TGGTCATTTT GGGGCGCTTA GGGGTGGGTG CCGGGGGGGC CGCTTTCCCT 120

CGTGAAGGTC GCTCCAGGAG TC ATG CGT ACA TTC GTT CAT TTT GCT CTG GAC 172

Met Arg Thr Phe Val His Phe Ala Leu Asp

271 GCA CTG ATG TTC CCG GCT CGC CGC CGT GCC GCA GTC ACG AGG CTC TCC Ala Leu Met Phe Pro Ala Arg Arg Ala Ala Val Thr Arg Leu Ser 220 -5 GAA CGC CTT TCA CTG TGT TTC TGT TTA CAT TCG CGT CTG CAA GAC CCG Glu Arg Leu Ser Leu Cys Phe Cys Leu His Ser Arg Leu Gln Asp Pro 10 GCG GCG CGA CCG AGG CCC TCT TGG Ala Ala Arg Pro Arg Pro Ser Trp 292 25 (2) INFORMATION FOR SEQ ID NO: 259: (i) SEQUENCE CHARACTERISTICS:

- - - (A) LENGTH: 338 base pairs
    - (B) TYPE: NUCLEIC ACID
    - (C) STRANDEDNESS: DOUBLE
    - (D) TOPOLOGY: LINEAR
  - (ii) MOLECULE TYPE: CDNA
  - (vi) ORIGINAL SOURCE:
    - (A) ORGANISM: Homo Sapiens
    - (F) TISSUE TYPE: Brain
  - (ix) FEATURE:
    - (A) NAME/KEY: other
    - (B) LOCATION: 131..273
    - (C) IDENTIFICATION METHOD: blastn
    - (D) OTHER INFORMATION: identity 92

region 120..262

id R10063

est

- (ix) FEATURE:
  - (A) NAME/KEY: other
  - (B) LOCATION: 35..101
  - (C) IDENTIFICATION METHOD: blastn
  - (D) OTHER INFORMATION: identity 100 region 26..92

id R10063

est

- (18) FEATURE:
  - (A) NAME/KEY: other
  - (3) LOCATION: 103..149
  - (C) IDENTIFICATION METHOD: blastn
  - (D) OTHER INFORMATION: identity 100

region 93..139

id R10063

- (ix) FEATURE:

  - (A) NAME/KEY: other (B) LOCATION: 275..312
  - (C) IDENTIFICATION METHOD: blastn
  - (D) OTHER INFORMATION: identity 97

272

region 266..303 id R10063

## (ix) FEATURE:

- (A) NAME/KEY: other(B) LOCATION: 131..273
- (C) IDENTIFICATION METHOD: blastn
- (D) OTHER INFORMATION: identity 92 region 130..272 id R12045

est

#### (ix) FEATURE:

- (A) NAME/KEY: other(B) LOCATION: 35..100
- (C) IDENTIFICATION METHOD: blastn
- (D) OTHER INFORMATION: identity 100 region 36..101 id R12045

est

#### (ix) FEATURE:

- (A) NAME/KEY: other
- (B) LOCATION: 103..149
- (C) IDENTIFICATION METHOD: blastn
- (D) OTHER INFORMATION: identity 100 region 103..149 id R12045

est

## (ix) FEATURE:

- (A) NAME/KEY: other
- (B) LOCATION: 3..35
- (C) IDENTIFICATION METHOD: blastn
- (D) OTHER INFORMATION: identity 96 region 5..37 id R12045

est

## (ix) FEATURE:

- (A) NAME/KEY: other
- (B) LOCATION: 131..273
- (C) IDENTIFICATION METHOD: blastn
- (D) OTHER INFORMATION: identity 92

region 125..267

id R12117

est

## (ix) FEATURE:

- (A) NAME/KEY: other
- (B) LOCATION: 5..100
- (C) IDENTIFICATION METHOD: blastn
- (D) OTHER INFORMATION: identity 98 region 1..96

id R12117

est

## (ix) FEATURE:

(A) NAME/KEY: other
(B) LOCATION: 103..149

TOTAL TOTAL BOTTON MODILED . . . .

(C) IDENTIFICATION METHOD: blastn (D) OTHER INFORMATION: identity 100 region 98..144 id R12117

est

#### (ix) FEATURE:

(A) NAME/KEY: other

(B) LOCATION: 131..273

(C) IDENTIFICATION METHOD: blastn

(D) OTHER INFORMATION: identity 92 region 102..244

id T79499

est

#### (ix) FEATURE:

(A) NAME/KEY: other

(B) LOCATION: 28..102

(C) IDENTIFICATION METHOD: blastn

(D) OTHER INFORMATION: identity 93

region 1..75 id T79499 est

#### (ix) FEATURE:

(A) NAME/KEY: other

(B) LOCATION: 104..149

(C) IDENTIFICATION METHOD: blastn

(D) OTHER INFORMATION: identity 97

region 76..121 id T79499

est

#### (ix) FEATURE:

(A) NAME/KEY: other

(B) LOCATION: 275..312

(C) IDENTIFICATION METHOD: blastn

(D) OTHER INFORMATION: identity 97

region 248..285 id T79499

est

#### (ix) FEATURE:

(A) NAME/KEY: other

(B) LOCATION: 109..178

(C) IDENTIFICATION METHOD: blastn

(D) OTHER INFORMATION: identity 95

region 109..178 id H17371

est

## (ix) FEATURE:

(A) NAME/KEY: other

(B) LOCATION: 275..332

(C) IDENTIFICATION METHOD: blastn

(D) OTHER INFORMATION: identity 100

region 283..340

id E17371

. ...

W	99/0	6552							27	4				РСТ/І	B98/01
			(B) (C)	NAME LOCA I DEN OTHE	TION TIFI	: 44 CATI	10 ON M	etho N:	iden regi	last tity on 4 1737	95 21	04			
	(i	ж) F	(B) (C)	RE: NAME LOCA IDEN OTHE	TION TIFI	: 42 CATI	22 ON M	4 ETHO N:	D: V scor	on H e 3. LVMT	8				
	(x	i) S	EQUE	NCE	DESC	RIPT	'ION:	SEQ	ID	NO:	259:				
AGCT	TACA	GT 1	CCT	AACCC	CC GP	CCCI	GCGC	GC#	ASCCO	CAC			a Al	CG CCG	56
				CTG Leu											104
				GCG Ala											152
				AAA Lys -20											200
				GGC Gly											248
				CAC His											296
				GCC Ala											338
(2)	INF	ORMA	TION	FOR	SEQ	ID	NO:	260:							

## (2) INFORMA

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 364 base pairs
- (3) TYPE: NUCLEIC ACID
- (C) STRANDEDNESS: DOUBLE
- (D) TOPOLOGY: LINEAR
- (ii) MOLECULE TYPE: CDNA
- (vi) ORIGINAL SOURCE:
  - (A) ORGANISM: Homo Sapiens
  - (F) TISSUE TYPE: Brain

(1x) FEATURE:

(A) NAME/KEY: other (B) LOCATION: 44..158 (C) I-DENTIFICATION METHOD: blastn (D) OTHER INFORMATION: identity 99 region 208..322 id AA017601 (ix) FEATURE: (A) NAME/KEY: other (B) LOCATION: 287..334 (C) IDENTIFICATION METHOD: blastn (D) OTHER INFORMATION: identity 97 region 451..498 id AA017601 est (ix) FEATURE: (A) NAME/KEY: sig\_peptide (B) LOCATION: 128..181 (C) IDENTIFICATION METHOD: Von Heijne matrix (D) OTHER INFORMATION: score 3.8 seq GXALGLLPSLAKA/ED (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 260: ACCCAGCTCC CGGAAGTGCG CCCGGAGCCG GCGCCGCGGG CCGAGTGTCC TGGTGAAGAC CTAGTTCTTG CCGGAGACAA TTCCACTGCA GAAGCACTTT ACTTAAAAGG ACTTGCCAGG 120 CTGGACA ATG CCC GTT GAC TTG GGG CAD GCC CTA GGC CTG CTG CCA TCG Met Pro Val Asp Leu Gly Xaa Ala Leu Gly Leu Leu Pro Ser 169 CTG GCG AAG GCC GAG GAC TCC CAG TTC TCA GAA TCA GAT GCT GCC CTT Leu Ala Lys Ala Glu Asp Ser Gln Phe Ser Glu Ser Asp Ala Ala Leu CAA GAG GAA CTC TCC AGC CCT GAG ACC GCA CGC CAG CTT TTC AGG CAG Gln Glu Glu Leu Ser Ser Pro Glu Thr Ala Arg Gln Leu Phe Arg Gln 265 TTC CGT TAC CAG GTG ATG TCT GGG CCT CAT GAG ACC TTG AAG CDA CTT Pne Arg Tyr Gln Val Met Ser Gly Pro His Glu Thr Leu Lys Xaa Leu 313 35 4.0 CGG AAG CTC TGT TTC CAG TGG CTA CAG CCA GAG GTT CAC ACC AAA GAG Arg Lys Leu Cys Phe Gln Trp Leu Gln Pro Glu Val His Thr Lys Glu 50 55 GGG  $Gi_{\mathcal{F}}$ 364

INFORMATION FOR SEQ ID NO: 261:

(1) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 433 base pairs
(B) TYPE: NUCLEIC ACID
(C) STRANDEDNESS: DOUBLE

(D) TOPOLOGY: LINEAR

## (ii) MOLECULE TYPE: CDNA

#### (vi) ORIGINAL SOURCE:

(A) ORGANISM: Homo Sapiens

(F) TISSUE TYPE: Brain

## (ix) FEATURE:

(A) NAME/KEY: other

(B) LOCATION: complement(324..433)

(C) IDENTIFICATION METHOD: blastn

(D) OTHER INFORMATION: identity 100 region 253..362 id H93008

## (ix) FEATURE:

(A) NAME/KEY: other

(B) LOCATION: complement(200..267).

(C) IDENTIFICATION METHOD: blastn

(D) OTHER INFORMATION: identity 92

region 423..490 id H93008

est

## (ix) FEATURE:

(A) NAME/KEY: other

(B) LOCATION: complement (159..205)

(C) IDENTIFICATION METHOD: blastn

(D) OTHER INFORMATION: identity 93

region 484..530

id H93008

est

## (ix) FEATURE:

(A) NAME/KEY: other

(B) LOCATION: complement(116..162)

(C) IDENTIFICATION METHOD: blastn

(D) OTHER INFORMATION: identity 91

region 526..572

id H93008

est

## (ix) FEATURE:

(A) NAME/KEY: other

(B) LOCATION: complement (259..299)

(C) IDENTIFICATION METHOD: blastn

(D) OTHER INFORMATION: identity 97

region 390..430

· id H93008

est

#### (ix) FEATURE:

(A) NAME/KEY: other

(B) LOCATION: complement (52..83)

(C) IDENTIFICATION METHOD: blastn

(D) OTHER INFORMATION: identity 90

region 602..633 id H93008 est

(ix) FEATURE:

(A) NAME/KEY: other

(B) LOCATION: 67..243

(C) IDENTIFICATION METHOD: blastn

(D) OTHER INFORMATION: identity 100

region 1..177 id AA146840 est

(ix) FEATURE:

(A) NAME/KEY: other(B) LOCATION: 332..417

(C) IDENTIFICATION METHOD: blastn

(D) OTHER INFORMATION: identity 100

region 269..354 id AA146840

est

(ix) FEATURE:

(A) NAME/KEY: other

(B) LOCATION: 242..299

(C) IDENTIFICATION METHOD: blastn

(D) OTHER INFORMATION: identity 100

region 177..234 id AA146840

est

(ix) FEATURE:

(A) NAME/KEY: other

(B) LOCATION: 299..334

(C) IDENTIFICATION METHOD: blastn

(D) OTHER INFORMATION: identity 100 region 235..270

id AA146840

est

(ix) FEATURE:

(A) NAME/KEY: other

(B) LOCATION: 85..299

(C) IDENTIFICATION METHOD: blastn

(D) OTHER INFORMATION: identity 99 region 1..215

id AA036893 est

(ix) FEATURE:

(A) NAME/KEY: other

(3) LOCATION: 299..412

(C) IDENTIFICATION METHOD: blastn

(D) OTHER INFORMATION: identity 97 region 216..329 id AA036893

est

(ix) FEATURE:

(A) NAME/KEY: other

(B) LOCATION: 98..243

(C) IDENTIFICATION METHOD: blastn (D) OTHER INFORMATION: identity 98

region 1..146

id T49176

#### (ix) FEATURE:

- (A) NAME/KEY: other
- (B) LOCATION: 242..299
- (C) IDENTIFICATION METHOD: blastn
- (D) OTHER INFORMATION: identity 100

region 146..203

id T49176

est

#### (ix) FEATURE:

- (A) NAME/KEY: other
- (B) LOCATION: 344..396
- (C) IDENTIFICATION METHOD: blastn
- (D) OTHER INFORMATION: identity 98

region 250..302

id T49176

est

#### (ix) FEATURE:

- (A) NAME/KEY: other
- (3) LOCATION: 299..349
- (C) IDENTIFICATION METHOD: blastn
- (D) OTHER INFORMATION: identity 96

region 204..254

id T49176

est

#### (ix) FEATURE:

- (A) NAME/KEY: other
- (B) LOCATION: 19..243
- (C) IDENTIFICATION METHOD: blastn
- (D) OTHER INFORMATION: identity 100

region 1..225

id H01262

est

#### (ix) FEATURE:

- (A) NAME/KEY: other
- (B) LOCATION: 242..296
- (C) IDENTIFICATION METHOD: blastn
- (D) OTHER INFORMATION: identity 100

region 225..279

id H01262

est

## (ix) FEATURE:

- (A) NAME/KEY: sig\_peptide
- (B) LOCATION: 17..232
- (C) IDENTIFICATION METHOD: Von Heijne matrix
- (D) OTHER INFORMATION: score 3.8

seq LMGLALAVYKCQS/MG

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 261:

										219						
							-70	rne	116	мет	Tyr	Met -65	Ala	Gly .	AAT AG Asn Ti	27 52 ir
-6(	)				-55	5	- 110	. va.	c cy:	-5(	c Me	t Al	a Trp	> Arc	A CCC g Pro -45	100
				-40	)		. Jei	. MIG	-35	: Phe	2 Lys	5 Met	: Leu	Glu -30		148
			-25			01	Oly	-20	vai	Tyr	Lei	: Ile	Gly -15	Asn	CTG Leu	196
		-10					-5	гÀ2	cys	GIN	Ser	Met 1	Gly	Leu		244
5	ACA Thr				10	7.2	200	nia	rue	15	Giu	Pro	Pro	Glu	Arg 20	292
	GAG Glu			25			Cys	rne	30	Glu	His	Glu	Lys	Ala 35	Ala	340
	GGT Gly		40				501	45	Leu	nıs	Pro	Ser	Leu 50	Ser	CCA Pro	388
GTG Val	GCT Ala	CCT Pro 55	CAG Gln	CAT His	ACT Thr	CTT Leu	AAA Lys 60	CTA Leu	ATC Ile	ACT Thr	TAT Tyr	GTT Val 65	AAA Lys	AAG Lys		433

# (2) INFORMATION FOR SEQ ID NO: 262:

- (i) SEQUENCE CHARACTERISTICS:
  - (A) LENGTH: 370 base pairs
  - (B) TYPE: NUCLEIC ACID
  - (C) STRANDEDNESS: DOUBLE
  - (D) TOPOLOGY: LINEAR
- (ii) MOLECULE TYPE: CDNA
- (vi) ORIGINAL SOURCE:
  - (A) ORGANISM: Homo Sapiens
  - (F) TISSUE TYPE: Brain
- (ix) FEATURE:
  - (A) NAME/KEY: other
  - (3) LOCATION: 2..250

  - (C) IDENTIFICATION METHOD: blastn
    (D) OTHER INFORMATION: identity 99 region 14..262 id N33874

#### (ix) FEATURE:

- (A) NAME/KEY: other
- (B) LOCATION: 78..270
- (C) IDENTIFICATION METHOD: blastn
- (D) OTHER INFORMATION: identity 98 region 1..193

id H01141

est

#### (ix) FEATURE:

- (A) NAME/KEY: other
- (B) LOCATION: 283..349
- (C) IDENTIFICATION METHOD: blastn
- (D) OTHER INFORMATION: identity 97

region 207..273

id H01141

est

## (ix) FEATURE:

. . . .

٠.

- (A) NAME/KEY: other
- (B) LOCATION: 284..366
- (C) IDENTIFICATION METHOD: blastn
- (D) OTHER INFORMATION: identity 92

region 320..402

id AA023741

est

#### (ix) FEATURE:

- (A) NAME/KEY: other
- (B) LOCATION: 74..270
- (C) IDENTIFICATION METHOD: blastn
- (D) OTHER INFORMATION: identity 100

region 2..198

id R27699

est

## (ix) FEATURE:

- (A) NAME/KEY: other
- (B) LOCATION: 320..349
- (C) IDENTIFICATION METHOD: blastn
- (D) OTHER INFORMATION: identity 93

region 253..282 id R27699

est

#### (ix) FEATURE:

- (A) NAME/KEY: other
- (B) LOCATION: complement(320..366)
- (C) IDENTIFICATION METHOD: blastn
- (D) OTHER INFORMATION: identity 97

region 282..328

id N33481

est

## (ix) FEATURE:

- (A) NAME/KEY: other
- (B) LOCATION: complement(283..322)
- (C) IDENTIFICATION METHOD: blastn
- (D) OTHER INFORMATION: identity 100

region 327..366

id N33481

(ix) FEATURE:

<ul> <li>(A) NAME/KEY: other</li> <li>(B) LOCATION: complement(235270)</li> <li>(C) IDENTIFICATION METHOD: blastn</li> <li>(D) OTHER INFORMATION: identity 97 region 379414 id N33481 est</li> </ul>	
(ix) FEATURE:  (A) NAME/KEY: sig_peptide  (B) LOCATION: 65217  (C) IDENTIFICATION METHOD: Von Heijne matrix  (D) OTHER INFORMATION: score 3.8  seq NVLFVAGLAFVIG/LE  (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 262:	
(X1) SEQUENCE DESCRIPTION. SEQ ID NO. 202:	
ACGACTCAGC TICCCACCCT GGGCTTTCCG AGGTGCTTTC GCCGCTGTCC CCACCA	стас 60
AGCC ATG ATC TCC TTA ACG GAC ACG CAG AAA ATT GGA ATG GGA TTA .  Met Ile Ser Leu Thr Asp Thr Gln Lys Ile Gly Met Gly Leu -50 -45 -40	
GGA TTT GGA GTG TTT TTC CTG TTC TTT GGA ATG ATT CTC TTT TTT G. Gly Phe Gly Val Phe Phe Leu Phe Phe Gly Met Ile Leu Phe Phe A -35 -30 -25	AC 157 sp
AAA GCA CTA CTG GCT ATT GGA AAT GTT TTA TTT GTA GCC GGC TTG G Lys Ala Leu Leu Ala Ile Gly Asn Val Leu Phe Val Ala Gly Leu A -20 -15 -10	
TTT GTA ATT GGT TTA GAA AGA ACA TTC AGA TTC TTC TTC CAA AAA C Phe Val Ile Gly Leu Glu Arg Thr Phe Arg Phe Phe Gln Lys H	
AAA ATG AAA GCT ACA GGT TTT TTT CTG GGT GGT GTA TTT GTA GTC C Lys Met Lys Ala Thr Gly Phe Phe Leu Gly Gly Val Phe Val Val L 15 20 25	
ATT GGT TGG CCT TTG ATA GGC ATG ATC TTC GAA ATT TAT GGA TTT Tile Gly Trp Pro Leu Ile Gly Met Ile Phe Glu Ile Tyr Gly Phe Post State	TT 349 The
CTC TTG TTC AGG GGC TTA GGG Leu Leu Phe Arg Gly Leu Gly 145 50	37(

## (2) INFORMATION FOR SEQ ID NO: 263:

- (i) SEQUENCE CHARACTERISTICS:
  - (A) LENGTH: 249 base pairs
    (B) TYPE: NUCLEIC ACID
    (C) STRANDEDNESS: DOUBLE
    (D) TOPOLOGY: LINEAR

(ii) MOLECULE TYPE: CDNA

## (vi) ORIGINAL SOURCE:

- (A) ORGANISM: Homo Sapiens
- (F) TISSUE TYPE: Brain

## (ix) FEATURE:

- (A) NAME/KEY: other
- (B) LOCATION: 112..249
- (C) IDENTIFICATION METHOD: blastn
- (D) OTHER INFORMATION: identity 97

region 153..290

id AA010288

est

#### (ix) FEATURE:

- (A) NAME/KEY: other
- (B) LOCATION: 112..218
- (C) IDENTIFICATION METHOD: blastn
- (D) OTHER INFORMATION: identity 96

region 101..207

id R26319

est

## (ix) FEATURE:

- (A) NAME/KEY: other
- (B) LOCATION: 208..247
- (C) IDENTIFICATION METHOD: blastn
- (D) OTHER INFORMATION: identity 92

region 198..237

id R26319

est

#### (ix) FEATURE:

- (A) NAME/KEY: other
- (B) LOCATION: 110..249
- (C) IDENTIFICATION METHOD: blastn
- (D) OTHER INFORMATION: identity 95

region 24..163

id W69087

est

#### (ix) FEATURE:

- (A) NAME/KEY: other
- (B) LOCATION: 112..247
- (C) IDENTIFICATION METHOD: blastn
- (D) OTHER INFORMATION: identity 98

region 103..238

id H01791

est

#### (ix) FEATURE:

- (A) NAME/KEY: other
- (B) LOCATION: complement(112..217)
- (C) IDENTIFICATION METHOD: blastn
- (D) OTHER INFORMATION: identity 98

region 287..392

id AA146617

est

## (ix) FEATURE:

		203	
(B) I (C) I	NAME/KEY: sig_peptid LOCATION: 91189 IDENTIFICATION METHO OTHER INFORMATION:	D: Von Heijne matrix	
(xi) SEQUE	NCE DESCRIPTION: SEQ	ID NO: 263:	
AAAAAAGCGA AGGCC	GGCCG GGCGGGGAAG GGA	AATGGCG AGGCAGAGT GCGGGGAGG	60
GAGTGGTCCT TAGCT		GCG GCC TCC GGC GCC CCA AGG Ala Ala Ser Gly Ala Pro Arg -30	114
		GTG GCC CCC CTC GCC GTC TTC Val Ala Pro Leu Ala Val Phe -15 ~10	162
		CAG AGG CTA GCG AGC GAG CCC Gln Arg Leu Ala Ser Glu Pro 1 5	210
	GCC GTG TCT CTG CCC Ala Val Ser Leu Pro 15		249
(i) SEQUEN (A) (3)	FOR SEQ ID NO: 264:  CE CHARACTERISTICS: LENGTH: 324 base pai TYPE: NUCLEIC ACID STRANDEDNESS: DOUBLE		
	TOPOLOGY: LINEAR	,	
(ii) MOLEC	CULE TYPE: CDNA		
(A)	NAL SOURCE: ORGANISM: Homo Sapie TISSUE TYPE: Brain	ens	
(3) (C) (D)	NAME/KEY: other LOCATION: 52178 IDENTIFICATION METHO OTHER INFORMATION:		
(3.9.) FEATI	IDF.		

(A) NAME/KEY: other

(B) LOCATION: 173..253
(C) IDENTIFICATION METHOD: blastn

(3) OTHER INFORMATION: identity 98 region 190..270 id W51974

	(ix) FEATURE:  (A) NAME/KEY: sig_peptide  (B) LOCATION: 49126  (C) IDENTIFICATION METHOD: Von Heijne matrix  (D) OTHER INFORMATION: score 3.6  seq ARSLLQFLRLVGQ/LK  (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 264:															
	()	(i) 5	SEQUE	ENCE	DESC	RIPT	rion:	SE(	Q ID	NO:	264:	:				
AAGO	GAGC	rtc (	GCCGG	CGGCC	CT GO	CTCC	GCCC/	A GC	CGGG	STCG	GTG	GCCG			T TCG a Ser	57
														CTG Leu		105
														GGC Gly	TGG Trp	153
														ATG Met		201
														AAC Asn 40	AAA Lys	249
									His					TGC Cys		297
			Ile				GAT Asp 65	Gly								324
(2)			EQUE (A) (B) (C)	NCE ( LENG TYP)	CHAR GTH: E: N	ACTE 157 UCLE DNES	NO: RIST bas IC A S: D INEA	ICS: e pa CID OUBL	irs							
	(	ii)	MOLE	CULE	TYP	E: C	DNA									
	(	vi)		ORG	ANIS	M: H	omo : Br		ens.							
,	(	ix)	(B) (C)	NAM LOC IDE	E/KE ATIO	N: c	other compl CION RMATI	emer METH	IOD: ide req	blas ntit jion		226				

(B) (C)	TURE: ) NAME/KEY: other ) LOCATION: complement(43156) ) IDENTIFICATION METHOD: blastn ) OTHER INFORMATION: identity 98 region 73186 id T23528 est	
(B) (C)	TURE:  NAME/KEY: other  LOCATION: complement(6156)  IDENTIFICATION METHOD: blastn  OTHER INFORMATION: identity 96  region 69219  id R50519  est	
(C)	CURE:  NAME/KEY: sig_peptide  LOCATION: 86133  IDENTIFICATION METHOD: Von Heijne matrix  OTHER INFORMATION: score 3.6  seq LAVLLVLFTLNIL/KS	
(xi) SEQU	ENCE DESCRIPTION: SEQ ID NO: 265:	
ACTGTATAAT RTGT	GTATAT KAAAATGTAA TTGATTTCAG YYGAAAGTAT TTTAAAGCTG	
	GGTTCT TTGCA ATG TGG TAT CTA GCT GTA TTA TTG GTT  Met Trp Tyr Leu Ala Val Leu Leu Val  -15	60 112
TTA TTT ACT TTA Leu Phe Thr Leu -5	AAC ATT TTG AAA AGC TTA TAC TGG CAG CCT GGG Asn Ile Leu Lys Ser Leu Tyr Trp Gln Pro Gly 1 5	157
(2) INFORMATION	FOR SEQ ID NO: 266:	
(i) SEQUEN (A) (B) (C)	NCE CHARACTERISTICS: LENGTH: 370 base pairs TYPE: NUCLEIC ACID STRANDEDNESS: DOUBLE TOPOLOGY: LINEAR	
(ii) MOLEC	CULE TYPE: CDNA	
(A)	INAL SOURCE: ORGANISM: Homo Sapiens TISSUE TYPE: Brain	
(B) (C)	JRE: NAME/KEY: other LOCATION: 4179 IDENTIFICATION METHOD: blastn OTHER INFORMATION: identity 92	

286

region 80..118 id T06923 est

ix	) FEATURE	

- (A) NAME/KEY: sig\_peptide
- (B) LOCATION: 197..322
- (C) IDENTIFICATION METHOD: Von Heijne matrix
- (D) OTHER INFORMATION: score 3.5

seq INSLLEXSSLSRC/LE

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 266:

ACATAAAGGA CASACGAGTC CTAATTGACA ACATCTAGTC TTTCTGGATG TTAAAGAGGT TGCCAGTGTA TGACAAAAGT AGAGTTAGTA AACTAATATA TTTTGTACAT TTTGTTTTAC 120 AAGTCCTAGG AAAGATTGTC TTCTGAAAAT TTGATGTCTT CTGGGTTGAW GGAGATGGGA 180 AGGGTTCTAG GCCAGA ATG TTC ACA TTT GGA AGA CTC TTT CAA ATT ATA ACT Met Phe Thr Phe Gly Arg Leu Phe Gln Ile Ile Thr -40 GTT GTT ACA TGT TTG CAG TTT ATT CAA GAC TGC TGT ATA CAT AGA 280 Val Val Thr Cys Leu Gln Phe Ile Gln Asp Cys Cys Ile His Ser Arg -25 -20 CAA ATT AAC TCC TTA CTT GAR RCA TCT AGT CTA TCT AGA TGT TTA GAA 328 Gln Ile Asn Ser Leu Leu Glu Xaa Ser Ser Leu Ser Arg Cys Leu Glu -10 GTG CCG ATG TAT GTY AAA TGT ATA GGT AGT AAA ATA CCA CTT 370 Val Pro Met Tyr Val Lys Cys Ile Gly Ser Lys Ile Pro Leu 5

#### (2) INFORMATION FOR SEQ ID NO: 267:

- (i) SEQUENCE CHARACTERISTICS:
  - (A) LENGTH: 301 base pairs
  - (B) TYPE: NUCLEIC ACID
  - (C) STRANDEDNESS: DOUBLE
  - (D) TOPOLOGY: LINEAR
- (ii) MOLECULE TYPE: CDNA
- (vi) ORIGINAL SOURCE:
  - (A) ORGANISM: Homo Sapiens
  - (F) TISSUE TYPE: Brain
- (ix) FEATURE:
  - (A) NAME/KEY: other
  - (B) LOCATION: 53..297
  - (C) IDENTIFICATION METHOD: blastn
  - (D) OTHER INFORMATION: identity 96 region 31..275 id HUM414A03B

(ix) FEATURE:  (A) NAME/KEY: other  (B) LOCATION: 22  (C) IDENTIFICATION  (D) OTHER INFORMAT:	METHOD: black
(ix) FEATURE: (A) NAME/KEY: other (B) LOCATION: 106 (C) IDENTIFICATION (D) OTHER INFORMATI	256
(ix) FEATURE:  (A) NAME/KEY: other  (B) LOCATION: 481  (C) IDENTIFICATION:  (D) OTHER INFORMATION	METHOD: blasts
(ix) FEATURE:  (A) NAME/KEY: sig_pe (B) LOCATION: 1162  (C) IDENTIFICATION N (D) OTHER INFORMATION  (xi) SEQUENCE DESCRIPTION:	METHOD: Von Heijne matrix N: score 3.5 seq VGTLCQLDWWIWG/GI
AAAATCAAGG CAGGGGATGG AGGCAAGTGG	GGGTCGCGCC TGGAGCGGAG CRTCGGCCTC 60
	TGAGATGGCT CGAGCCTAAC ATTCC ATG 118
ATC CAG GAT CGT GAC AGA TGT GCA Ile Gln Asp Arg Asp Arg Cys Ala -50 -45	GIN ATA ATA ATA VAL ATA ATA VAL -40 -35
GGT AAT TTG GAA CCA CGA GGC ACC Gly Asn Leu Glu Pro Arg Gly Thr -30	-25 -20
TGT CTG CCT GGA TGT GTG GGA ACT Cys Leu Pro Gly Cys Val Gly Thr -15	CTC TGC CAA CTT GAT TGG TGG ATC Leu Cys Gln Leu Asp Trp Trp Ile -10 -5
TGG GGG GGG ATC CAC CCC CAC CCC 7. Trp Gly Gly Ile His Pro His Pro 1 5	ACG AGG AAA GCC TGG 301 Thr Arg Lys Ala Trp 10

(i) SEQUENCE CHARACTERISTICS:

(i) SEQUENCE CHARACTERISTICS:

(B (C	) LENGTH: 404 base pairs ) TYPE: NUCLEIC ACID ) STRANDEDNESS: DOUBLE ) TOPOLOGY: LINEAR	
(ii) MOL	ECULE TYPE: CDNA	
(A	GINAL SOURCE:  ORGANISM: Homo Sapiens TISSUE TYPE: Brain	
(B	TURE:  1) NAME/KEY: other  2) LOCATION: 261404  2) IDENTIFICATION METHOD: fasta  3) OTHER INFORMATION: identity 100  region 1144  id HSU16126  vrt	
(E (C	ATURE:  A) NAME/KEY: sig_peptide  B) LOCATION: 261353  C) IDENTIFICATION METHOD: Von Heijne matrix  D) OTHER INFORMATION: score 11.3  Seq LLLCLLWIGYSQG/TT	
(xi) SE(	QUENCE DESCRIPTION: SEQ ID NO: 268:	
AGGATTTCTC CCC	GGATGCTC TCCGACTAAC ATGGATGTCC CACCATTCCT TGCAGTGGAA	60
GGTTGTTCCT TG	GCGCAGTG AGTGAAGAAC ATGCAGCGAT TGCTAATGGG TTTGGGAAGC	120
GGAGACTCCT TC	CTCTCTCT ATGACCATGC CGTGATCGTG TCTGCGGTCA CCACTCGACG	180
CATCCTCATT TC	TACCCGAA CCCAGGAGCC GAACGCTAGA TCGGGGAAGT GGGTGCCGTG	240
CGTGTGGGCA CA	GAAACACC ATG AAG ATT ATT TTC CCG ATT CTA AGT AAT CCA Met Lys Ile Ile Phe Pro Ile Leu Ser Asn Pro -30 -25	293
	GC ACC GTT AAA CTC CTG CTC TGT TTA CTG TGG ATT GGA rg Thr Val Lys Leu Leu Cys Leu Leu Trp Ile Gly -15 -10 -5	341
	GA ACC ACA CAT GTA TTA AGA TTT GGT GGT ATT TTT GAA ly Thr Thr His Val Leu Arg Phe Gly Gly Ile Phe Glu 1 5 10	389
TAT GTG GAA T Tyr Val Glu S 15		404
(2) INFORMATI	ON FOR SEQ ID NO: 269:	

WO 99/06552 PCT/IB98/01236

(A) LENGTH: 249 base pairs(B) TYPE: NUCLEIC ACID(C) STRANDEDNESS: DOUBLE(D) TOPOLOGY: LINEAR

(ii) MOLECULE TYPE: CDNA

### (vi) ORIGINAL SOURCE:

- (A) ORGANISM: Homo Sapiens
- (F) TISSUE TYPE: Brain

#### (ix) FEATURE:

(A) NAME/KEY: other

(B) LOCATION: 52..250

(C) IDENTIFICATION METHOD: fasta

(D) OTHER INFORMATION: identity 99 region 2..200 id HS7B2 vrt

## (ix) FEATURE:

(A) NAME/KEY: other

(B) LOCATION: 14..250

(C) IDENTIFICATION METHOD: blastn

(D) OTHER INFORMATION: identity 98 region 24..260 id R14271

est

# (ix) FEATURE:

(A) NAME/KEY: other
(B) LOCATION: 14..250

(C) IDENTIFICATION METHOD: blastn

(D) OTHER INFORMATION: identity 98

region 25..261 id R18347

est

### (ix) FEATURE:

(A) NAME/KEY: other

(B) LOCATION: 14..233

(C) IDENTIFICATION METHOD: blastn

(D) OTHER INFORMATION: identity 97

region 43..262 id H10233

est

### (ix) FEATURE:

(A) NAME/KEY: other

(B) LOCATION: 14..240

(C) IDENTIFICATION METHOD: blastn

(D) OTHER INFORMATION: identity 99

region 44..270 id HSC0IE021

est

## (ix) FEATURE:

(A) NAME/KEY: other

(B) LOCATION: 42..250

(C) IDENTIFICATION METHOD: blastn

(D) OTHER INFORMATION: identity 98

290

region 1..209 id HSCZSC021

{	ix	FEATURE	:
١	_LA.	LEWIOUS	4

- (A) NAME/KEY: sig\_peptide
- (B) LOCATION: 79..156
- (C) IDENTIFICATION METHOD: Von Heijne matrix
- (D) OTHER INFORMATION: score 6.6

seq LFWLASGWTPAFA/YS

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 269:

AAGTTCGCCC GTNTCCTGGC CTGACCCCCA CCAAGGCCCA TACCGCAGTA GGCTCCTCGG 60

GCTGCCCCTC GGTTGACA ATG GTC TCC AGG ATG GTC TCT ACC ATG CTA TCT

Met Val Ser Arg Met Val Ser Thr Met Leu Ser

-25

-20

GGC CTA CTG TTT TGG CTG GCA TCT GGA TGG ACT CCA GCA TTT GCT TAC

Gly Leu Leu Phe Trp Leu Ala Ser Gly Trp Thr Pro Ala Phe Ala Tyr

-15

-10

-5

159

AGC CCC CGG ACC CCT GAC CGG GTC TCA GAA GCA GAT ATC CAG AGG CTG 207
Ser Pro Arg Thr Pro Asp Arg Val Ser Glu Ala Asp Ile Gln Arg Leu
5 10 15

CTT CAT GGT GTT ATG GAG CAA TTG GGC ATT GCC AGG CCC CGG
Leu His Gly Val Met Glu Gln Leu Gly Ile Ala Arg Pro Arg
20 25 30

## (2) INFORMATION FOR SEQ ID NO: 270:

- (i) SEQUENCE CHARACTERISTICS:
  - (A) LENGTH: 316 base pairs
  - (B) TYPE: NUCLEIC ACID
  - (C) STRANDEDNESS: DOUBLE
  - (D) TOPOLOGY: LINEAR
- (ii) MOLECULE TYPE: CDNA
- (vi) ORIGINAL SOURCE:
  - (A) ORGANISM: Homo Sapiens
  - (F) TISSUE TYPE: Brain
- (ix) FEATURE:
  - (A) NAME/KEY: other
  - (B) LOCATION: 212..311
  - (C) IDENTIFICATION METHOD: fasta
  - (D) OTHER INFORMATION: identity 93 region 1..101 id HSSCOASN

vrt

- (ix) FEATURE:
  - (A) NAME/KEY: other
  - (B) LOCATION: 243..311
  - (C) IDENTIFICATION METHOD: blastn

			(D)	OTH	ER I	NFOR	MATI	: AO	reg	ion	y 94 60 5265	128				
	(	ix)	(B) (C)	URE: NAM. LOC. IDEI OTHI	OITA TIT	N: 1 ICAT	87 ION	245 METH	ide: reg	ntit	y 91 56	3				
	(	ix)	(B) (C)	URE: NAMI LOCA IDEN	ATION ATIF	N: 2	69 ION 1	METH	ide reg	ntity	y 100 19	0 91				
	(.	ix)	(B)	URE: NAME LOCA IDEN OTHE	ATIO!  TIF]	N: 1 [CAT]	79 [ON: N	250 METH(	DD: N	ce 4.	. 8	ne ma SGLA)				
	(;	xi)	SEQUE	ENCE	DES	CRIP	NOI	: SE(	Q ID	NO:	270:	:				
GA(	GTTA'	TTA	TCTG	CSTST	rc co	GATA	GGAT	G CC	rctt	rgtc	TTC	ACCT	GCC	ATTC	CCGCTG	60
															CCCTCT	120
			GCCT													173
TG let	ACC Thr	GCA Ala	ACC Thr	CTT Leu -20	GCC Ala	GCT Ala	GCC Ala	GCT Ala	GAC Asp -15	ATC Ile	GCT Ala	ACC Thr	ATG Met	GTC Val -10	TCC Ser	226
GC ly	AGC Ser	AGC Ser	GGC Gly -5	CTC Leu	GCC Ala	GNC Xaa	GCC Ala	CGT Arg 1	CTC Leu	CTG Leu	TCG Ser	CGC Arg 5	AST Xaa	TCC Ser	TCC Ser	274
GC Ys	CGC Arg 10	AGA Arg	ATG Met	GAA Glu	TTC Phe	GGC Gly 15	ATT Ile	GTT Val	CCT Pro	ACA Thr	CAG G1n 20	CCA Pro	CGG Arg			316
2)			(≘)		HARI TH: : AN	ACTER 37 a MINO	RISTI umino ACIE	ICS: aci	.ds							
	( ;	ii) :	MOLE:													

- (vi) ORIGINAL SOURCE:
  - (A) ORGANISM: Homo Sapiens
  - (F) TISSUE TYPE: Brain
- (ix) FEATURE:
  - (A) NAME/KEY: sig\_peptide
  - (B) LOCATION: -14..-1
  - (C) IDENTIFICATION METHOD: Von Heijne matrix
  - (D) OTHER INFORMATION: score 10.8

seq LLLLGLCLGLSLC/VG

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 271:

Met Leu Leu Leu Gly Leu Cys Leu Gly Leu Ser Leu Cys Val Gly
-10 -5

Ser Gln Glu Glu Ala Gln Ser Trp Gly His Ser Ser Glu Gln Asp Gly
5 10 15

Leu Arg Val Pro Arg 20

- (2) INFORMATION FOR SEQ ID NO: 272:
  - (i) SEQUENCE CHARACTERISTICS:
    - (A) LENGTH: 79 amino acids
    - (B) TYPE: AMINO ACID
    - (D) TOPOLOGY: LINEAR
  - (ii) MOLECULE TYPE: PROTEIN
  - (vi) ORIGINAL SOURCE:
    - (A) ORGANISM: Homo Sapiens
    - (F) TISSUE TYPE: Brain
  - (ix) FEATURE:
    - (A) NAME/KEY: sig\_peptide
    - (B) LOCATION: -26..-1
    - (C) IDENTIFICATION METHOD: Von Heijne matrix
    - (D) OTHER INFORMATION: score 10.8

seq VLLFFVLLGMSQA/GS

- (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 272:
- Met Glu Asn Gly Gly Ala Gly Thr Leu Gln Ile Arg Gln Val Leu Leu
  -25 -20 -15

Phe Phe Val Leu Gly Met Ser Gln Ala Gly Ser Glu Thr Gly Asn -10 -5 1 5

Phe Leu Val Met Glu Glu Leu Gln Ser Gly Ser Phe Val Gly Asn Leu 10 15 20

Ala Lys Thr Leu Gly Leu Glu Val Ser Glu Leu Ser Ser Arg Gly Ala 25 30 Arg Val Val Ser Asn Asp Asn Lys Glu Cys Leu Gln Leu Asp Thr
40 45 50

- (2) INFORMATION FOR SEQ ID NO: 273:
  - (i) SEQUENCE CHARACTERISTICS:
    - (A) LENGTH: 129 amino acids
    - (B) TYPE: AMINO ACID
    - (D) TOPOLOGY: LINEAR
  - (ii) MOLECULE TYPE: PROTEIN
  - (vi) ORIGINAL SOURCE:
    - (A) ORGANISM: Homo Sapiens
    - (F) TISSUE TYPE: Brain
  - (ix) FEATURE:
    - (A) NAME/KEY: sig\_peptide
    - (B) LOCATION:  $-12\overline{6}..-1$
    - (C) IDENTIFICATION METHOD: Von Heijne matrix
    - (D) OTHER INFORMATION: score 10 seq LKLLLFLSTELQA/SQ
  - (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 273:

Met Arg Gly Pro Glu Pro Gly Pro Gln Pro Thr Met Glu Gly Asp Val

Leu Asp Thr Leu Glu Ala Leu Gly Tyr Lys Gly Pro Leu Leu Glu Glu -110 -105 -100 -100

Gln Ala Leu Thr Lys Ala Ala Glu Gly Gly Leu Ser Ser Pro Glu Phe
-90 -85 -80

Ser Glu Leu Cys Ile Trp Leu Gly Ser Gln Ile Lys Ser Leu Cys Asn
-75 -70 -65

Leu Glu Ser Ile Thr Ser Ala Gly Arg Asp Asp Leu Glu Ser Fhe

Gln Leu Glu Ile Ser Gly Phe Leu Lys Glu Met Ala Cys Pro Tyr Ser -45 -40 -35

Val Leu Ile Ser Gly Asp Ile Lys Asp Arg Leu Lys Lys Glu Asp -20 -25

Cys Leu Lys Leu Leu Phe Leu Ser Thr Glu Leu Gln Ala Ser Gln -10 -5

Ile

- (2) INFORMATION FOR SEQ ID NO: 274:
  - (i) SEQUENCE CHARACTERISTICS:
    - (A) LENGTH: 44 amino acids
    - (B) TYPE: AMINO ACID

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- (D) TOPOLOGY: LINEAR
- (ii) MOLECULE TYPE: PROTEIN
- (vi) ORIGINAL SOURCE:
  - (A) ORGANISM: Homo Sapiens
  - (F) TISSUE TYPE: Brain
- (ix) FEATURE:
  - (A) NAME/KEY: sig peptide
  - (B) LOCATION: -26..-1
  - · (C) IDENTIFICATION METHOD: Von Heijne matrix
    - (D) OTHER INFORMATION: score 9.6

seq WLIALASWSWALC/RI

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 274:

Met Glu Lys Ser Trp Met Leu Trp Asn Phe Val Glu Arg Trp Leu Ile
-25
-20
-15

Ala Leu Ala Ser Trp Ser Trp Ala Leu Cys Arg Ile Ser Leu Leu Pro-10 -5 5

Leu Ile Val Thr Phe His Leu Tyr Gly Gly Ser Gly

- (2) INFORMATION FOR SEQ ID NO: 275:
  - (i) SEQUENCE CHARACTERISTICS:
    - (A) LENGTH: 89 amino acids
    - (B) TYPE: AMINO ACID
    - (D) TOPOLOGY: LINEAR
  - (ii) MOLECULE TYPE: PROTEIN
  - (vi) ORIGINAL SOURCE:
    - (A) ORGANISM: Homo Sapiens
    - (F) TISSUE TYPE: Brain
  - (ix) FEATURE:
    - (A) NAME/KEY: sig peptide
    - (B) LOCATION: -36..-1
    - (C) IDENTIFICATION METHOD: Von Heijne matrix
    - (D) OTHER INFORMATION: score 9.5

seq LGLLLLARHWCIA/GV

- (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 275:
- Met Gln Gln Thr Arg Thr Glu Ala Val Ala Gly Ala Phe Ser His Cys
  -35 -25

Leu Gly Phe Cys Gly Met Arg Leu Gly Leu Leu Leu Leu Ala Arg His
-20 -15 -10 -5

Trp Cys Ile Ala Gly Val Phe Pro Gln Lys Phe Asp Gly Asp Ser Ala  $1 \hspace{1.5cm} 5 \hspace{1.5cm} 10$ 

Tyr Val Gly Met Ser Asp Gly Asn Pro Glu Leu Leu Ser Thr Ser Gl $_{
m H}$ 20

Thr Tyr Asn Gly Gln Ser Glu Asn Asn Glu Asp Tyr Glu Ile Pro Pro 35

Ile Thr Pro Pro Asn Leu Pro Glu Ala

- (2) INFORMATION FOR SEQ ID NO: 276:
  - (i) SEQUENCE CHARACTERISTICS:
    - (A) LENGTH: 53 amino acids
    - (B) TYPE: AMINO ACID
    - (D) TOPOLOGY: LINEAR
  - (ii) MOLECULE TYPE: PROTEIN
  - (vi) ORIGINAL SOURCE:
    - (A) ORGANISM: Homo Sapiens
    - (F) TISSUE TYPE: Brain
  - (ix) FEATURE:
    - (A) NAME/KEY: sig\_peptide
    - (B) LOCATION: -24..-1
    - (C) IDENTIFICATION METHOD: Von Heijne matrix
    - (D) OTHER INFORMATION: score 9.1

seq LVVFLLLPLASGP/QV

- (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 276:
- Met Glu Lys Gly Asn Ala Phe Leu Lys Asn Arg Leu Val Val Phe Leu -15

Leu Leu Pro Leu Ala Ser Gly Pro Gln Val Lys Arg Lys Ser Glu Ile

Thr Lys Leu Ile Lys Ala Thr Arg Ile Ile Cys Leu Phe Asn Lys Fne

Ser Arg Gly Asn Gly

- (2) INFORMATION FOR SEQ ID NO: 277:
  - (i) SEQUENCE CHARACTERISTICS:
    - (A) LENGTH: 79 amino acids
    - (3) TYPE: AMINO ACID
    - (D) TOPOLOGY: LINEAR
  - (ii) MOLECULE TYPE: PROTEIN
  - (vi) ORIGINAL SOURCE:
    - (A) ORGANISM: Homo Sapiens
    - (F) TISSUE TYPE: Brain

- (ix) FEATURE:
  - (A) NAME/KEY: sig\_peptide
  - (B) LOCATION: -24..-1
  - (C) IDENTIFICATION METHOD: Von Heijne matrix
  - (D) OTHER INFORMATION: score 9

seq LLMLIVFHAASMA/LQ

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 277:

Met Phe Pro Phe Asn Gln Ala Gly Leu Pro Thr Leu Leu Met Leu Ile -20 -15 -10

Val Phe His Ala Ala Ser Met Ala Leu Gln Arg Leu Phe Leu Phe Ala -5 1 5

Leu Val Trp His Ser Lys Pro Ser Gly Leu Met Thr Gly Lys Leu Glu 10 15 20

Ser Gln Ile Pro His Glu Lys Leu Thr His Ile Ser Val Met His Gly 25 30 35 40

Pro Leu Ser Ser His His Ser Tyr Thr His Ile His Leu Phe Leu 45 50 55

- (2) INFORMATION FOR SEQ ID NO: 278:
  - (i) SEQUENCE CHARACTERISTICS:
    - (A) LENGTH: 99 amino acids
    - (B) TYPE: AMINO ACID
    - (D) TOPOLOGY: LINEAR
  - (ii) MOLECULE TYPE: PROTEIN
  - (vi) ORIGINAL SOURCE:
    - (A) ORGANISM: Homo Sapiens
    - (F) TISSUE TYPE: Brain
  - (ix) FEATURE:
    - (A) NAME/KEY: sig\_peptide
    - (B) LOCATION: -76..-1
    - (C) IDENTIFICATION METHOD: Von Heijne matrix
    - (D) OTHER INFORMATION: score 8.8

seq SLLLWMSSLPSLG/EK

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 278:

Met Thr Ser Arg Ser Leu Arg Arg Cys Ser Cys Leu Arg Val Thr His

Asn Lys Glu Ile Leu Ala Ser Thr Val Ser Leu Gly Val Glu Gly Tyr -60 -55 -50 -45

Met Leu Gly Gly Gly Ser Arg Ile Asn Ser Ser Asn Leu Asn Asp Gly
-40 -35 -33

Glu Glu Glu Cys Ser Pro Asp Ser Leu Leu Val Trp Lys Lys Ser
-25 -20 -15

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Leu Leu Trp Met Ser Ser Leu Pro Ser Leu Gly Glu Lys Tyr Phe -5

Lys Arg Ile Leu Arg Trp Arg Glu His Trp Lys Ser Ser Gly Pro Ile 10 15

Pro Leu Trp

- (2) INFORMATION FOR SEQ ID NO: 279:
  - (i) SEQUENCE CHARACTERISTICS:
    - (A) LENGTH: 68 amino acids
    - (B) TYPE: AMINO ACID
    - (D) TOPOLOGY: LINEAR
  - (ii) MOLECULE TYPE: PROTEIN
  - (vi) ORIGINAL SOURCE:
    - (A) ORGANISM: Homo Sapiens
    - (F) TISSUE TYPE: Brain
  - (ix) FEATURE:
    - (A) NAME/KEY: sig\_peptide
    - (B) LOCATION: -53..-1
    - (C) IDENTIFICATION METHOD: Von Heijne matrix
    - (D) OTHER INFORMATION: score 8.8
      - seq ILLLLTVLPCIXM/GQ
  - (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 279:

Met Trp Thr Ala Ser Ala Met Asp Phe Arg Thr Cys Ile Ala Ser Xaa

Leu Pro Ala Leu Cys Tyr Val Gln Ala Cys Arg Ala Leu Met Ile Ala -30

Ala Ser Val Leu Gly Leu Pro Ala Ile Leu Leu Leu Leu Thr Val Leu -15

Pro Cys Ile Kaa Met Gly Gln Glu Pro Gly Val Ala Lys Tyr Arg Kaa

Ala Gln Leu Ala

- (2) INFORMATION FOR SEQ ID NO: 280:
  - (1) SEQUENCE CHARACTERISTICS:
    - (A) LENGTH: 86 amino acids
    - (B) TYPE: AMINO ACID
    - (D) TOPOLOGY: LINEAR
  - (ii) MOLECULE TYPE: PROTEIN
  - (2) ORIGINAL SOURCE:

- (A) ORGANISM: Homo Sapiens
  (F) TISSUE TYPE: Brain
- (ix) FEATURE:
  - (A) NAME/KEY: sig\_peptide
  - (B) LOCATION: -45..-1
  - (C) IDENTIFICATION METHOD: Von Heijne matrix
  - (D) OTHER INFORMATION: score 8.5

seq FALLSLSHPTCQA/GA

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 280:

Met Gly Pro Pro Pro Thr His Ile Lys Tyr Leu His Leu Asn Ile Tyr
-45
-35
-30

Cys Asn Gly Lys Ser Thr Ala Pro Gly Ile Arg Ser His Ser Leu Gly -25 -20 -15

Phe Ala Leu Leu Ser Leu Ser His Pro Thr Cys Gln Ala Gly Ala Pro
-10 -5 1

Ala Ala Leu Pro Ser Leu Trp Ser Trp Cys Ser Arg Gly Ala Arg
5 10 15

Val Arg Val Gly Arg Met Leu Ser His Leu Tyr Thr Cys Gly Trp Tyr 20 25 30 35

Asp His Asn Pro His Gly

- (2) INFORMATION FOR SEQ ID NO: 281:
  - (i) SEQUENCE CHARACTERISTICS:
    - (A) LENGTH: 19 amino acids
    - (B) TYPE: AMINO ACID
    - (D) TOPOLOGY: LINEAR
  - (ii) MOLECULE TYPE: PROTEIN
  - (vi) ORIGINAL SOURCE:
    - (A) ORGANISM: Homo Sapiens
    - (F) TISSUE TYPE: Brain
  - (ix) FEATURE:
    - (A) NAME/KEY: sig\_peptide
    - (B) LOCATION: -16..-1
    - (C) IDENTIFICATION METHOD: Von Heijne matrix
    - (D) OTHER INFORMATION: score 8.5

seq LLTFLAFTTLLFA/PP

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 281:

Met Phe Cys Leu Leu Thr Phe Leu Ala Phe Thr Thr Leu Leu Phe Ala
-15 -5

Pro Pro Trp

```
(2) INFORMATION FOR SEQ ID NO: 282:
```

- (i) SEQUENCE CHARACTERISTICS:
  - (A) LENGTH: 80 amino acids
  - (B) TYPE: AMINO ACID
  - (D) TOPOLOGY: LINEAR
- (ii) MOLECULE TYPE: PROTEIN
- (vi) ORIGINAL SOURCE:
  - (A) ORGANISM: Homo Sapiens
  - (F) TISSUE TYPE: Brain
- (ix) FEATURE:
  - (A) NAME/KEY: sig\_peptide
  - (B) LOCATION: -29..-1
  - (C) IDENTIFICATION METHOD: Von Heijne matrix
  - (D) OTHER INFORMATION: score 8.4

seq LKCLLAVLSSLFA/AI

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 282:

Met His Cys Gly Ser Thr Pro Gly Leu Cys Pro Cys Trp Val Pro Phe

Leu Lys Cys Leu Leu Ala Val Leu Ser Ser Leu Phe Ala Ala Ile Ser -10 -5 1

Val Asp Arg Leu Tyr Leu Ser Phe Cys Ser Asn Cys Ser Glu Ile Tyr 5 10 15

Leu Trp Pro Pro Ser Phe Pro Ala Pro Pro Ser Pro Val Val Leu Leu 20 25 30 35

Val Phe Leu Cys Pro His Gly Thr Ser Leu Ser Phe Leu Lys Leu Pro

# (2) INFORMATION FOR SEQ ID NO: 283:

- (i) SEQUENCE CHARACTERISTICS:
  - (A) LENGTH: 23 amino acids
  - (B) TYPE: AMINO ACID
  - (D) TOPOLOGY: LINEAR
- (ii) MOLECULE TYPE: PROTEIN
- (vi) ORIGINAL SOURCE:
  - (A) ORGANISM: Homo Sapiens
  - (F) TISSUE TYPE: Brain
- (ix) FEATURE:
  - (A) NAME/KEY: sig\_peptide
  - (B) LOCATION: -16..-1
  - (C) IDENTIFICATION METHOD: Von Heijne matrix
  - (D) OTHER INFORMATION: score 8.3

# seq VCSALLLLGIVSS/KP

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 283:

Met Asn Leu Val Cys Ser Ala Leu Leu Leu Gly Ile Val Ser Ser
-15 -10 -5

Lys Pro Tyr Met Arg Lys Arg
1 5

- (2) INFORMATION FOR SEQ ID NO: 284:
  - (i) SEQUENCE CHARACTERISTICS:
    - (A) LENGTH: 47 amino acids
    - (B) TYPE: AMINO ACID
    - (D) TOPOLOGY: LINEAR
  - (ii) MOLECULE TYPE: PROTEIN
  - (vi) ORIGINAL SOURCE:
    - (A) ORGANISM: Homo Sapiens
    - (F) TISSUE TYPE: Brain
  - (ix) FEATURE:
    - (A) NAME/KEY: sig\_peptide
    - (B) LOCATION: -35..-1
    - (C) IDENTIFICATION METHOD: Von Heijne matrix
    - (D) OTHER INFORMATION: score 8.3 seq AAMLIGLLAWLQT/VP
  - (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 284:

Met Ser Val Leu Asp Asp Arg Gln Arg Asp Ile Leu Val Val Gln Lys
-35 -20 -25

Arg His Ser Ser Leu Glu Ala Ala Met Leu Ile Gly Leu Leu Ala Trp
-15
-10
-5

Leu Gln Thr Val Pro Ala His Gly Cys Gln Phe Leu Pro Ile Arg
1 5 10

- (2) INFORMATION FOR SEQ ID NO: 285:
  - (i) SEQUENCE CHARACTERISTICS:
    - (A) LENGTH: 38 amino acids
    - (B) TYPE: AMINO ACID
    - (D) TOPOLOGY: LINEAR
  - (ii) MOLECULE TYPE: PROTEIN
  - (vi) ORIGINAL SOURCE:
    - (A) ORGANISM: Homo Sapiens
    - (F) TISSUE TYPE: Brain
  - (ix) FEATURE:

(A) NAME/KEY: sig\_peptide

(B) LOCATION: -20..-1

- (C) IDENTIFICATION METHOD: Von Heijne matrix
- (D) OTHER INFORMATION: score 8.3 seq LLIICHYLPLSLC/IP

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 285:

Met Gly Val Asn Gly Arg Arg Leu Leu Ile Ile Cys His Tyr Leu Pro -10

Leu Ser Leu Cys Ile Pro Ile Pro Ser His Ile Asn Ser Leu Pro Arg

Asn Thr Pro Pro Val Arg

- (2) INFORMATION FOR SEQ ID NO: 286:
  - (i) SEQUENCE CHARACTERISTICS:
    - (A) LENGTH: 43 amino acids
    - (B) TYPE: AMINO ACID
    - (D) TOPOLOGY: LINEAR
  - (ii) MOLECULE TYPE: PROTEIN
  - (vi) ORIGINAL SOURCE:
    - (A) ORGANISM: Homo Sapiens
    - (F) TISSUE TYPE: Brain
  - (ix) FEATURE:
    - (A) NAME/KEY: sig\_peptide
    - (B) LOCATION: -31..-1
    - (C) IDENTIFICATION METHOD: Von Heijne matrix
    - (D) OTHER INFORMATION: score 8.2 seq LECLLLYLAESSG/LR
  - (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 286:

Met Lys Leu Arg Glu Cys Pro Ala Leu Arg Trp Ser Gln Leu Ser Gln

His Lys Leu Glu Cys Leu Leu Leu Tyr Leu Ala Glu Ser Ser Gly Leu -5

Arg Thr Gly Asn Val Gly Val Leu His Pro Arg 10

- (2) INFORMATION FOR SEQ ID NO: 287:
  - (i) SEQUENCE CHARACTERISTICS:
    - (A) LENGTH: 136 amino acids
    - (B) TYPE: AMINO ACID
    - (D) TOPOLOGY: LINEAR

- (ii) MOLECULE TYPE: PROTEIN
- (vi) ORIGINAL SOURCE:
  - (A) ORGANISM: Homo Sapiens
  - (F) TISSUE TYPE: Brain
- (ix) FEATURE:
  - (A) NAME/KEY: sig\_peptide
  - (B) LOCATION: -109..-1
  - (C) IDENTIFICATION METHOD: Von Heijne matrix
  - (D) OTHER INFORMATION: score 8.2 seq LLRLPQLPPXCSA/GE
- (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 287:
- Met Asp Pro Arg Gly Ile Leu Lys Ala Phe Pro Lys Arg Gln Lys Ile
  -105
  -100
  -95
- His Ala Asp Ala Ser Ser Lys Val Leu Ala Lys Ile Pro Arg Arg Glu .
  -90 -85 -80
- Glu Gly Glu Glu Ala Glu Glu Trp Leu Ser Ser Leu Arg Ala His Val
  -75 -70 -65
- Val Arg Thr Gly Ile Gly Arg Ala Arg Ala Glu Leu Phe Glu Lys Gln
  -60 -55 -50
- Ile Val Gln His Gly Gly Gln Leu Cys Pro Ala Gln Gly Pro Gly Val
  -45 -35 -30
- Thr His Ile Val Val Asp Glu Gly Met Asp Tyr Glu Arg Ala Leu Arg
  -25 -20 -15
- Leu Leu Arg Leu Pro Gln Leu Pro Pro Xaa Cys Ser Ala Gly Glu Val
- Ser Leu Ala Glu Leu Val Pro Ser Gly Glu Glu Ala Gly Gly Cys Ser 5 10 15
- Trp Ile Gln His Leu His Pro Ser
- (2) INFORMATION FOR SEQ ID NO: 288:
  - (i) SEQUENCE CHARACTERISTICS:
    - (A) LENGTH: 26 amino acids
    - (B) TYPE: AMINO ACID
    - (D) TOPOLOGY: LINEAR
  - (ii) MOLECULE TYPE: PROTEIN
  - (vi) ORIGINAL SOURCE:
    - (A) ORGANISM: Homo Sapiens
    - (F) TISSUE TYPE: Brain
  - (ix) FEATURE:
    - (A) NAME/KEY: sig\_peptide
    - (B) LOCATION: -21..-1

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(C) IDENTIFICATION METHOD: Von Heijne matrix

(D) OTHER INFORMATION: score 8

seq LFLVAVLVKVAEA/RK

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 288:

Met Phe Trp Lys Leu Ser Leu Ser Leu Phe Leu Val Ala Val Leu Val -10

Lys Val Ala Glu Ala Arg Lys Asn Arg Ser

- (2) INFORMATION FOR SEQ ID NO: 289:
  - (i) SEQUENCE CHARACTERISTICS:
    - (A) LENGTH: 26 amino acids
    - (B) TYPE: AMINO ACID
    - (D) TOPOLOGY: LINEAR
  - (ii) MOLECULE TYPE: PROTEIN
  - (vi) ORIGINAL SOURCE:
    - (A) ORGANISM: Homo Sapiens
    - (F) TISSUE TYPE: Brain
  - (ix) FEATURE:
    - (A) NAME/KEY: sig\_peptide
    - (B) LOCATION: -18..-1
    - (C) IDENTIFICATION METHOD: Von Heijne matrix
    - (D) OTHER INFORMATION: score 7.9

seq LFSLLVLQSMATG/AT

(xi) SEQUENCE DESCRIPTION: SEO ID NO: 289:

Met Ala Phe Leu Gly Leu Phe Ser Leu Leu Val Leu Gln Ser Met Ala -10

Thr Gly Ala Thr Phe Pro Glu Glu Ala Pro 1

- (2) INFORMATION FOR SEQ ID NO: 290:
  - (i) SEQUENCE CHARACTERISTICS:
    - (A) LENGTH: 70 amino acids
    - (B) TYPE: AMINO ACID
    - (D) TOPOLOGY: LINEAR
  - (ii) MOLECULE TYPE: PROTEIN
  - (vi) ORIGINAL SOURCE:
    - (A) ORGANISM: Homo Sapiens
    - (F) TISSUE TYPE: Brain
  - (1x) FEATURE:
    - (A) NAME/KEY: sig peptide

- (B) LOCATION: -18..-1
- (C) IDENTIFICATION METHOD: Von Heijne matrix
- (D) OTHER INFORMATION: score 7.9 seq LFSLLVLQSMATG/AT
- (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 290:

Met Ala Phe Leu Gly Leu Phe Ser Leu Leu Val Leu Gln Ser Met Ala
-15 -10 -5

Thr Gly Ala Thr Phe Pro Glu Glu Ala Ile Ala Asp Leu Ser Val Asn
1 5 10

Met Tyr Asn Arg Leu Arg Ala Val Gly Ser Trp Arg Arg Glu Gly Ala 15 20 25 30

Ser Arg Gln Ile Ala Ser Cys Leu Pro Ala Phe Leu Leu His Leu Pro
35 40 45

Leu Thr His Thr His Gly

- (2) INFORMATION FOR SEQ ID NO: 291:
  - (i) SEQUENCE CHARACTERISTICS:
    - (A) LENGTH: 103 amino acids
    - (B) TYPE: AMINO ACID
    - (D) TOPOLOGY: LINEAR
  - (ii) MOLECULE TYPE: PROTEIN
  - (vi) ORIGINAL SOURCE:
    - (A) ORGANISM: Homo Sapiens
    - (F) TISSUE TYPE: Brain
  - (ix) FEATURE:
    - (A) NAME/KEY: sig\_peptide
    - (B) LOCATION: -55..-1
    - (C) IDENTIFICATION METHOD: Von Heijne matrix
    - (D) OTHER INFORMATION: score 7.8 seq ALLVALLFTLIHR/RR
  - (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 291:

Met Ser Phe Ser Leu Asn Phe Thr Leu Pro Ala Asn Thr Thr Ser Ser
-55 -45 -45

Pro Val Thr Gly Gly Lys Glu Thr Asp Cys Gly Pro Ser Leu Gly Leu
-35 -30 -25

Ala Ala Gly Ile Pro Leu Leu Val Ala Thr Ala Leu Leu Val Ala Leu
-20 -15 -10

Leu Phe Thr Leu Ile His Arg Arg Arg Ser Ser Ile Glu Ala Met Glu
-5 5

Glu Ser Asp Arg Pro Cys Glu Ile Ser Glu Ile Asp Asp Asn Pro Lys

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15 20 25

Ile Ser Glu Asn Pro Arg Arg Ser Pro Thr His Glu Lys Asn Thr Met 30 35 40

Gly Ala Gln Glu Ala Arg Trp

- (2) INFORMATION FOR SEQ ID NO: 292:
  - (i) SEQUENCE CHARACTERISTICS:
    - (A) LENGTH: 82 amino acids
    - (B) TYPE: AMINO ACID
    - (D) TOPOLOGY: LINEAR
  - (ii) MOLECULE TYPE: PROTEIN
  - (vi) ORIGINAL SOURCE:
    - (A) ORGANISM: Homo Sapiens
    - (F) TISSUE TYPE: Brain
  - (ix) FEATURE:
    - (A) NAME/KEY: sig\_peptide
    - (B) LOCATION: -80..-1
    - (C) IDENTIFICATION METHOD: Von Heijne matrix
    - (D) OTHER INFORMATION: score 7.7

seq LVLFLSLALLVTP/TS

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 292:

Met Ser Thr Trp Tyr Leu Ala Leu Asn Lys Ser Tyr Lys Asn Lys Asp -80 -75 -70 -65

Ser Val Arg Ile Tyr Leu Ser Leu Cys Thr Val Ser Ile Lys Phe Thr
-60 -55 -50

Tyr Phe His Asp Ile Gln Thr Asn Cys Leu Thr Thr Trp Lys His Ser -45 -40 -35

Arg Cys Arg Phe Tyr Trp Ala Phe Gly Gly Ser Ile Leu Gln His Ser -30 -25 -20

Val Asp Pro Leu Val Leu Phe Leu Ser Leu Ala Leu Leu Val Thr Pro
-15 -10 -5

Thr Ser

- (2) INFORMATION FOR SEQ ID NO: 293:
  - (i) SEQUENCE CHARACTERISTICS:
    - (A) LENGTH: 43 amino acids
    - (B) TYPE: AMINO ACID
    - (D) TOPOLOGY: LINEAR
  - (ii) MOLECULE TYPE: PROTEIN

- (vi) ORIGINAL SOURCE:
  - (A) ORGANISM: Homo Sapiens
  - (F) TISSUE TYPE: Brain
- (ix) FEATURE:
  - (A) NAME/KEY: sig\_peptide
  - (B) LOCATION: -19..-1
  - (C) IDENTIFICATION METHOD: Von Heijne matrix
  - (D) OTHER INFORMATION: score 7.7

seq LQLLCCIFTLVLQ/HY

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 293:

Met Ala Ile Gly Ile Ser Leu Gln Leu Leu Cys Cys Ile Phe Thr Leu
-15 -10 -5

Val Leu Gln His Tyr Leu Leu Gly Ser His Pro Tyr Ile Thr Cys Ile 1 5 10

His Ser Glm Leu Leu Leu Asp Ile Glm Glm 15 20

- (2) INFORMATION FOR SEQ ID NO: 294:
  - (i) SEQUENCE CHARACTERISTICS:
    - (A) LENGTH: 74 amino acids
    - (B) TYPE: AMINO ACID
    - (D) TOPOLOGY: LINEAR
  - (ii) MOLECULE TYPE: PROTEIN
  - (vi) ORIGINAL SOURCE:
    - (A) ORGANISM: Homo Sapiens
    - (F) TISSUE TYPE: Brain
  - (ix) FEATURE:
    - (A) NAME/KEY: sig\_peptide
    - (B) LOCATION: -19..-1
    - (C) IDENTIFICATION METHOD: Von Heijne matrix
    - (D) OTHER INFORMATION: score 7.6

seq LLNLLLLSLFAGL/DP

- (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 294:
- Met Gln Ala Thr Ser Asn Leu Leu Asn Leu Leu Leu Leu Ser Leu Phe -15 -10 -5
- Ala Gly Leu Asp Pro Ser Lys Asn Lys Lys Arg Gly Ser Ser Phe Ser
  1 5 10
- Phe Lys Phe Pro Leu Leu Asp Asp Thr Pro Phe Leu Xaa Ser Arg Ile 15 20 25
- Glu Asn Ser Ala Thr His His Leu His Tyr Gly Leu Asn Met Ile Leu 30 40 45

Trp Val Asn Trp Lys Pro Lys Leu Thr Leu
50

- (2) INFORMATION FOR SEQ ID NO: 295:
  - (i) SEQUENCE CHARACTERISTICS:
    - (A) LENGTH: 34 amino acids
    - (B) TYPE: AMINO ACID
    - (D) TOPOLOGY: LINEAR
  - (ii) MOLECULE TYPE: PROTEIN
  - (vi) ORIGINAL SOURCE:
    - (A) ORGANISM: Homo Sapiens
    - (F) TISSUE TYPE: Brain
  - (ix) FEATURE:
    - (A) NAME/KEY: sig\_peptide
    - (B) LOCATION: -31..-1
    - (C) IDENTIFICATION METHOD: Von Heijne matrix
    - (D) OTHER INFORMATION: score 7.6 seq VTLLCGWPGSHWC/AP
  - (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 295:
- Met Met Lys Trp Lys Pro Glu Asp Leu Gly Ser Val Pro Cys Glu Ala
  -30 -25 -20
- Proc Ser Val Thr Leu Leu Cys Gly Trp Pro Gly Ser His Trp Cys Ala -15 -5 1

Pro Pro

- (2) INFORMATION FOR SEQ ID NO: 296:
  - (i) SEQUENCE CHARACTERISTICS:
    - (A) LENGTH: 78 amino acids
    - (B) TYPE: AMINO ACID
    - (D) TOPOLOGY: LINEAR
    - (ii) MOLECULE TYPE: PROTEIN
    - (vi) ORIGINAL SOURCE:
      - (A) ORGANISM: Homo Sapiens
      - (F) TISSUE TYPE: Brain
    - (1x) FEATURE:
      - (A) NAME/KEY: sig\_peptide
      - (B) LOCATION: -19..-1
      - (C) IDENTIFICATION METHOD: Von Heijne matrix
      - (D) OTHER INFORMATION: score 7.6

seq LLNLLLLSLFAGL/DP

Mi) SEQUENCE DESCRIPTION: SEQ ID NO: 296:

Met Gln Ala Thr Ser Asn Leu Leu Asn Leu Leu Leu Leu Ser Leu Phe
-15
-10
-5

- Ala Gly Leu Asp Pro Ser Lys Thr Gln Ile Ser Pro Lys Glu Gly Trp  $1 \hspace{1cm} 5 \hspace{1cm} 10$
- Gln Val Tyr Ser Ser Ala Gln Asp Pro Asp Gly Arg Cys Ile Cys Thr 15 20 25
- Val Val Ala Pro Glu Gln Asn Leu Cys Ser Arg Asp Ala Lys Ser Arg 30 40 45
- Gln Leu Arg Gln Leu Leu Glu Lys Val Gln Asn Met Ser Arg
  50
  55
- (2) INFORMATION FOR SEQ ID NO: 297:
  - (i) SEQUENCE CHARACTERISTICS:
    - (A) LENGTH: 80 amino acids
    - (B) TYPE: AMINO ACID
    - (D) TOPOLOGY: LINEAR
  - (ii) MOLECULE TYPE: PROTEIN
  - (vi) ORIGINAL SOURCE:
    - (A) ORGANISM: Homo Sapiens
    - (F) TISSUE TYPE: Brain
  - (ix) FEATURE:
    - (A) NAME/KEY: sig\_peptide
    - (B) LOCATION: -48..-1
    - (C) IDENTIFICATION METHOD: Von Heijne matrix
    - (D) OTHER INFORMATION: score 7.5 seq FVILLLFIFTVVS/LV
  - (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 297:
- Met Ala Ser Ser His Trp Asn Glu Thr Thr Thr Ser Val Tyr Gln Tyr
  -45
  -40
  -35
- Leu Gly Phe Gln Val Gln Lys Ile Tyr Pro Phe His Asp Asn Trp Asn
  -30
  -25
  -20
- Thr Ala Cys Phe Val Ile Leu Leu Phe Ile Phe Thr Val Val Ser
  -15 -10 -5
- Leu Val Val Leu Ala Phe Leu Tyr Glu Val Leu Asp Cys Cys Cys Cys 1 5 10 15
- Val Lys Asn Lys Thr Val Lys Asp Leu Lys Ser Glu Pro Asn Pro Arg 20 25 30
- (2) INFORMATION FOR SEQ ID NO: 298:
  - (i) SEQUENCE CHARACTERISTICS:
    (A) LENGTH: 35 amino acids

(B) TYPE: AMINO ACID (D) TOPOLOGY: LINEAR

- (ii) MOLECULE TYPE: PROTEIN
- (vi) ORIGINAL SOURCE:
  - (A) ORGANISM: Homo Sapiens
  - (F) TISSUE TYPE: Brain
- (ix) FEATURE:
  - (A) NAME/KEY: sig\_peptide
  - (B) LOCATION: -33..-1
  - (C) IDENTIFICATION METHOD: Von Heijne matrix
  - (D) OTHER INFORMATION: score 7.4 seq ITCCVLLLLNCSG/VW
- (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 298:

Met Leu Trp Phe Ser Gly Val Gly Ala Leu Ala Glu Arg Tyr Cys Arg -30 -25 -20

Arg Ser Pro Gly Ile Thr Cys Cys Val Leu Leu Leu Leu Asn Cys Ser

Gly Val Trp

(2) INFORMATION FOR SEQ ID NO: 299:

- (i) SEQUENCE CHARACTERISTICS:
  - (A) LENGTH: 31 amino acids
  - (B) TYPE: AMINO ACID
  - (D) TOPOLOGY: LINEAR
- (ii) MOLECULE TYPE: PROTEIN
- (vi) ORIGINAL SOURCE:
  - (A) ORGANISM: Homo Sapiens
  - (F) TISSUE TYPE: Brain
- (ix) FEATURE:
  - (A) NAME/KEY: sig\_peptide
  - (B) LOCATION: -25..-1
  - (C) IDENTIFICATION METHOD: Von Heijne matrix
  - (D) OTHER INFORMATION: score 7.3

seq LIFFLNVTQLVRG/RG

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 299:

Net Lei Phe Leu Gln Met Gly Lys Gln Ser Trp Thr Leu Ile Phe Phe

her: Ash Val Thr Gln Leu Val Arg Gly Arg Gly Pro Gly Gly Arg -5

- (2) INFORMATION FOR SEQ ID NO: 300:
  - (i) SEQUENCE CHARACTERISTICS:
    - (A) LENGTH: 36 amino acids
    - (B) TYPE: AMINO ACID
    - (D) TOPOLOGY: LINEAR
  - (ii) MOLECULE TYPE: PROTEIN
  - (vi) ORIGINAL SOURCE:
    - (A) ORGANISM: Homo Sapiens
    - (F) TISSUE TYPE: Brain
  - (ix) FEATURE:
    - (A) NAME/KEY: sig\_peptide
    - (B) LOCATION: -27..-1
    - (C) IDENTIFICATION METHOD: Von Heijne matrix
    - (D) OTHER INFORMATION: score 7.2 seq LLLGLCSPPXXSL/AS
  - (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 300:
- Met Glu Leu Arg Xaa Xaa Pro Pro Gly Gly Arg Glu Val Gln Leu Leu
  -25 -20 -15
- Leu Gly Leu Cys Ser Pro Pro Xaa Xaa Ser Leu Ala Ser Phe Pro Lys
  -10 -5 1 5

Ala Ala Gln Met

- (2) INFORMATION FOR SEQ ID NO: 301:
  - (i) SEQUENCE CHARACTERISTICS:
    - (A) LENGTH: 24 amino acids
    - (3) TYPE: AMINO ACID
    - (D) TOPOLOGY: LINEAR
  - (ii) MOLECULE TYPE: PROTEIN
  - (vi) ORIGINAL SOURCE:
    - (A) ORGANISM: Homo Sapiens
    - (F) TISSUE TYPE: Brain
  - (ix) FEATURE:
    - (A) NAME/KEY: sig\_peptide
    - (B) LOCATION: -14..-1
    - (C) IDENTIFICATION METHOD: Von Heijne matrix
    - (D) OTHER INFORMATION: score 7

seq LWSLLSSSGSHFG/IP

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 301:

Met Leu Trp Ser Leu Leu Ser Ser Ser Gly Ser His Phe Gly Ile Pro

His His Thr Phe Pro Gln Glu Gly
5

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```
(2) INFORMATION FOR SEQ ID NO: 302:
```

- (i) SEQUENCE CHARACTERISTICS:
  - (A) LENGTH: 112 amino acids
  - (B) TYPE: AMINO ACID
  - (D) TOPOLOGY: LINEAR
- (ii) MOLECULE TYPE: PROTEIN
- (vi) ORIGINAL SOURCE:
  - (A) ORGANISM: Homo Sapiens
  - (F) TISSUE TYPE: Brain
- (ix) FEATURE:
  - (A) NAME/KEY: sig\_peptide
  - (B) LOCATION: -52..-1
  - (C) IDENTIFICATION METHOD: Von Heijne matrix
  - (D) OTHER INFORMATION: score 7

seq SVWLCLLCYFAFP/FQ

- (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 302:
- Met Asp Ile Ser Gly Leu Ile Pro Gly Leu Val Ser Thr Phe Ile Leu -45
- Leu Ser Xaa Ser Asp His Tyr Gly Arg Lys Phe Pro Met Ile Leu Ser -30
- Ser Val Gly Ala Leu Ala Thr Ser Val Trp Leu Cys Leu Leu Cys Tyr
- Phe Ala Phe Pro Phe Gln Leu Leu Ile Ala Ser Thr Phe Ile Gly Ala
- Phe Xaa Gly Asn Tyr Thr Thr Phe Trp Gly Ala Cys Phe Ala Tyr Ile 20
- Val Asp Gln Cys Lys Glu Xaa Xaa Gln Lys Thr Ile Arg Ile Ala Ile
- Ile Asp Phe Leu Leu Gly Leu Val Thr Gly Leu Thr Val Leu Ser Ser 50 45 55
- (2) INFORMATION FOR SEQ ID NO: 303:
  - (i) SEQUENCE CHARACTERISTICS:
    - (A) LENGTH: 36 amino acids
    - (B) TYPE: AMINO ACID
    - (D) TOPOLOGY: LINEAR
  - (ii) MOLECULE TYPE: PROTEIN
  - (vi) ORIGINAL SOURCE:
    - (A) ORGANISM: Homo Sapiens
    - (F) TISSUE TYPE: Brain

- (ix) FEATURE:
  - (A) NAME/KEY: sig\_peptide
  - (B) LOCATION: -30..-1
  - (C) IDENTIFICATION METHOD: Von Heijne matrix
  - (D) OTHER INFORMATION: score 7

seq LFVILLITSLIFC/SL

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 303:

Met Xaa Val Phe Phe Ser Lys Asn Arg Phe Glu Met Tyr Phe Ser Leu
-30 -25 -20 -15

Leu Leu Phe Val Ile Leu Leu Ile Thr Ser Leu Ile Phe Cys Ser Leu
-10 -5 1

Tyr Val Ala Arg

- (2) INFORMATION FOR SEQ ID NO: 304:
  - (i) SEQUENCE CHARACTERISTICS:
    - (A) LENGTH: 34 amino acids
    - (B) TYPE: AMINO ACID
    - (D) TOPOLOGY: LINEAR
  - (ii) MOLECULE TYPE: PROTEIN
  - (vi) ORIGINAL SOURCE:
    - (A) ORGANISM: Homo Sapiens
    - (F) TISSUE TYPE: Brain
  - (ix) FEATURE:
    - (A) NAME/KEY: sig\_peptide
    - (B) LOCATION: -23..-1
    - (C) IDENTIFICATION METHOD: Von Heijne matrix
    - (D) OTHER INFORMATION: score 6.9

seg SLSLLASHHSVSC/SN

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 304:

Met Pro Val Pro Ala Cys Trp Ile Ser Ser Ser Leu Ser Leu Ala
-20
-15
-10

Ser His His Ser Val Ser Cys Ser Asn Ile Phe Leu Asn Phe Asn Pro
-5 1 5

Asp Arg

- (2) INFORMATION FOR SEQ ID NO: 305:
  - (i) SEQUENCE CHARACTERISTICS:
    - (A) LENGTH: 59 amino acids
    - (B) TYPE: AMINO ACID

(D) TOPOLOGY: LINEAR

- (ii) MOLECULE TYPE: PROTEIN
- (vi) ORIGINAL SOURCE:
  - (A) ORGANISM: Homo Sapiens
  - (F) TISSUE TYPE: Brain
- (ix) FEATURE:
  - (A) NAME/KEY: sig\_peptide
  - (B) LOCATION: -21..-1
  - (C) IDENTIFICATION METHOD: Von Heijne matrix
  - (D) OTHER INFORMATION: score 6.9

seq LLACGSLLPGLWO/HL

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 305:

Met Cys Pro Val Phe Ser Lys Gln Leu Leu Ala Cys Gly Ser Leu Leu
-20 -15 -10

Pro Gly Leu Tro Gln His Leu Thr Ala Asn His Trp Pro Pro Phe Ser -5 5 10

Xaa Phe Leu Cys Thr Val Cys Ser Gly Ser Ser Glu Gln Ile Ser Glu
15 20 25

Tyr Thr Ala Ser Ala Thr Pro Pro Leu Cys Leu 30 35

- (2) INFORMATION FOR SEQ ID NO: 306:
  - (i) SEQUENCE CHARACTERISTICS:
    - (A) LENGTH: 128 amino acids
    - (B) TYPE: AMINO ACID
    - (D) TOPOLOGY: LINEAR
  - (ii) MOLECULE TYPE: PROTEIN
  - (vi) ORIGINAL SOURCE:
    - (A) ORGANISM: Homo Sapiens
    - (F) TISSUE TYPE: Brain
  - (ix) FEATURE:
    - (A) NAME/KEY: sig\_peptide
    - (B) LOCATION: -76..-1
    - (C) IDENTIFICATION METHOD: Von Heijne matrix
    - (D) OTHER INFORMATION: score 6.9

seq LLPLSAWPPWAWH/HH

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 306:

Met Ala Leu Thr Ile His Gly Glu Arg Met Arg Pro Asp Trp Glu Ser
-75 -70 -65

Fro Trp Ile Thr Ser Ser Gln Ala Gln Ser Leu Ser Leu Gly Gly Ser -60 -55 -50 -45

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Pro Ser Ser Arg Gly Pro Leu Val Pro Arg Gly Glu Tyr Leu Ala Ser
-40 -35 -30

- Cys Pro Glu Gly Val Arg Ser His Ser His Leu Leu Pro Arg Ser Leu
  -25 -20 -15
- Leu Pro Leu Ser Ala Trp Pro Pro Trp Ala Trp His His Gly Pro
  -10 -5
- Gly Thr Gln Ser Leu Val Gly Cys Leu Cys Ala Met Ser Pro Leu Leu 5 10 15 20
- Pro Thr His Leu Ser Leu Pro Val Leu Glu Pro Ser Gly Thr Pro Ala 25 30 35
- Leu Lys Asp Arg Arg Pro Cys Glu Val Gly Ile Pro Ile Pro Pro Arg
  40 45 50
- (2) INFORMATION FOR SEQ ID NO: 307:
  - (i) SEQUENCE CHARACTERISTICS:
    - (A) LENGTH: 95 amino acids
    - (B) TYPE: AMINO ACID
    - (D) TOPOLOGY: LINEAR
  - (ii) MOLECULE TYPE: PROTEIN
  - (vi) ORIGINAL SOURCE:
    - (A) ORGANISM: Homo Sapiens
    - (F) TISSUE TYPE: Brain
  - (ix) FEATURE:
    - (A) NAME/KEY: sig\_peptide
    - (B) LOCATION: -92..-1
    - (C) IDENTIFICATION METHOD: Von Heijne matrix
    - (D) OTHER INFORMATION: score 6.8

seq ILIASSLPTLSHP/AP

- (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 307:
- Met Ala Ala Arg Phe Arg Cys Gly His Leu Cys Val Pro Glu Val Pro -90 -85 -80
- Arg Gly Pro Ala Ser His Ala Glu Gly Gly Gly Gly Arg Leu Ser Arg
  -75 -70 -65
- Lys Ala Ala His Gln Ala Gln Leu Cys Trp Arg Ala Gly Gly Asp Gly -50 -55 -50 -45
- Arg Gly Asn Phe Asn Pro Met Asn Phe Leu Val Ala Gly Thr Phe Ala
  -40
  -35
  -30
- Ser Ser Cys His Ser Pro Pro Leu Leu Trp Ser Leu Pro Pro Arg Ile
  -25 -20 -15
- Leu Ile Ala Ser Ser Leu Pro Thr Leu Ser His Pro Ala Pro Gly
  -10 -5 1

315

```
(2) INFORMATION FOR SEQ ID NO: 308:
```

- (i) SEQUENCE CHARACTERISTICS:
  - (A) LENGTH: 87 amino acids
  - (B) TYPE: AMINO ACID
  - (D) TOPOLOGY: LINEAR
- (11) MOLECULE TYPE: PROTEIN
- (vi) ORIGINAL SOURCE:
  - (A) ORGANISM: Homo Sapiens
  - (F) TISSUE TYPE: Brain
- (ix) FEATURE:
  - (A) NAME/KEY: sig\_peptide
  - (B) LOCATION: -29..-1
  - (C) IDENTIFICATION METHOD: Von Heijne matrix
  - (D) OTHER INFORMATION: score 6.8

seq VLSLICSCFYTQP/HP

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 308:

Met Ala Ser Thr Ile Ser Ala Tyr Lys Glu Lys Met Lys Glu Leu Ser
-25 -20 -15

Val Leu Ser Leu Ile Cys Ser Cys Phe Tyr Thr Gln Pro His Pro Asn

Thr Val Tyr Gln Tyr Gly Asp Met Glu Val Lys Gln Leu Asp Lys Arg
5 10

Ala Ser Gly Gln Ser Phe Glu Val Ile Leu Lys Ser Pro Ser Asp Leu 20 30 35

Ser Pro Glu Ser Pro Met Leu Ser Ser Pro Pro Lys Lys Lys Asp Thr 40 45 50

Ser Leu Glu Glu Leu Gln Lys 55

(2) INFORMATION FOR SEQ ID NO: 309:

- (i) SEQUENCE CHARACTERISTICS:
  - (A) LENGTH: 120 amino acids
  - (B) TYPE: AMINO ACID
  - (D) TOPOLOGY: LINEAR
- (11) MOLECULE TYPE: PROTEIN
- (vi) ORIGINAL SOURCE:
  - (A) ORGANISM: Homo Sapiens
  - (F) TISSUE TYPE: Brain
- (1x) FEATURE:
  - (A) NAME/KEY: sig\_peptide
  - (5) LOCATION:  $-11\overline{4}..-1$

- (C) IDENTIFICATION METHOD: Von Heijne matrix
- (D) OTHER INFORMATION: score 6.7 seq LIPMAILLGQTQS/NS
- (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 309:

Met Leu Gln Val Tyr Gly Lys Pro Val Tyr Gln Gly His Arg Ser Thr -110 -105 -100

Leu Lys Lys Gly Pro Tyr Leu Arg Phe Asn Ser Pro Ser Pro Lys Ser
-95
-90
-85

Arg Pro Gln Arg Pro Lys Val Ile Glu Arg Val Lys Gly Thr Lys Val
-80 -75 -70

Lys Ser Ile Arg Thr Gln Thr Asp Phe Tyr Ala Thr Lys Pro Lys Lys
-65 -60 -55

Met Asp Ser Lys Met Lys His Ser Val Pro Val Leu Pro His Gly Asp
-50
-45
-40
-35

Gin Gln Tyr Leu Phe Ser Pro Ser Arg Glu Met Pro Thr Phe Ser Gly
-30
-25
-20

Thr Leu Glu Gly His Leu Ile Pro Met Ala Ile Leu Leu Gly Gln Thr -15 -10 -5

Gln Ser Asn Ser Asp Thr Met Pro

- (2) INFORMATION FOR SEQ ID NO: 310:
  - (i) SEQUENCE CHARACTERISTICS:
    - (A) LENGTH: 127 amino acids
    - (B) TYPE: AMINO ACID
    - (D) TOPOLOGY: LINEAR
  - (ii) MOLECULE TYPE: PROTEIN
  - (vi) ORIGINAL SOURCE:
    - (A) ORGANISM: Homo Sapiens
    - (F) TISSUE TYPE: Brain
  - (ix) FEATURE:
    - (A) NAME/KEY: sig\_peptide
    - (B) LOCATION: -118..-1
    - (C) IDENTIFICATION METHOD: Von Heijne matrix
    - (D) OTHER INFORMATION: score 6.7

seq LLFAKLFGHLTSA/RR

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 310:

Met Ser Val Leu Glu Ile Ser Gly Met Ile Met Asn Arg Val Asn Ser -115 -110 -105

His Ile Pro Gly Ile Gly Tyr Gln Ile Phe Gly Asn Ala Val Ser Leu
-100 -95 -90

lie Leu Gly Leu Thr Pro Phe Val Phe Arg Leu Ser Gln Ala Thr Asp

Leu Giu Gln Leu Thr Ala His Ser Ala Ser Glu Leu Tyr Val Ile Ala -65

Phe Gly Ser Asn Glu Asp Val Ile Val Leu Ser Met Val Ile Ile Ser -50 -45

Phe Val Val Arg Val Ser Leu Val Trp Ile Phe Phe Phe Leu Leu Cys

Val Ala Glu Arg Thr Tyr Lys Gln Arg Leu Leu Phe Ala Lys Leu Phe -15

Gly His Leu Thr Ser Ala Arg Arg Ala Arg Lys Ser Glu Val Pro

# (2) INFORMATION FOR SEQ ID NO: 311:

- (i) SEQUENCE CHARACTERISTICS:
  - (A) LENGTH: 71 amino acids
  - (B) TYPE: AMINO ACID
  - (D) TOPOLOGY: LINEAR
- (ii) MOLECULE TYPE: PROTEIN
- (vi) ORIGINAL SOURCE:
  - (A) ORGANISM: Homo Sapiens
  - (F) TISSUE TYPE: Brain
- (ix) FEATURE:
  - (A) NAME/KEY: sig\_peptide
  - (B) LOCATION: -69..-1
  - (C) IDENTIFICATION METHOD: Von Heijne matrix
  - (D) OTHER INFORMATION: score 6.7 seq FFKLLLLGAMCSG/AR
- (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 311:

Met Cys Lys Gly Ile Lys Ala Gly Asp Thr Cys Glu Lys Leu Val Gly -65 -60

Tyr Ser Ala Val Tyr Arg Val Cys Phe Gly Met Ala Cys Phe Phe Phe -45

lie Phe Cys Leu Leu Thr Leu Lys Ile Asn Asn Ser Lys Ser Cys Arg -30

Ala His Ile His Asn Gly Phe Trp Phe Phe Lys Leu Leu Leu Gly -15

Ala Met Cys Ser Gly Ala Arg

- (2) INFORMATION FOR SEQ ID NO: 312:
  - (i) SEQUENCE CHARACTERISTICS:
    - (A) LENGTH: 114 amino acids
    - (B) TYPE: AMINO ACID
    - (D) TOPOLOGY: LINEAR
  - (ii) MOLECULE TYPE: PROTEIN
  - (vi) ORIGINAL SOURCE:
    - (A) ORGANISM: Homo Sapiens
    - (F) TISSUE TYPE: Brain
  - (ix) FEATURE:
    - (A) NAME/KEY: sig peptide
    - (B) LOCATION: -104..-1
    - (C) IDENTIFICATION METHOD: Von Heijne matrix
    - (D) OTHER INFORMATION: score 6.6 seq HFSHVVWFHPTWA/QQ
  - (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 312:
- Met Ser Asp Ser Ala Gly Gly Arg Ala Gly Leu Arg Arg Tyr Pro Lys
  -100 -95 -90
- Leu Pro Val Trp Val Val Glu Asp His Gln Glu Val Leu Pro Phe Ile
  -85
  -80
  -75
- Tyr Arg Ala Ile Gly Ser Lys His Leu Pro Ala Ser Asn Val Ser Phe
  -70 -65 -60
- Leu His Phe Asp Ser His Pro Asp Leu Leu Ile Pro Val Asn Met Pro
  -55 -50 -45
- Ala Asp Thr Val Phe Asp Lys Glu Thr Leu Phe Gly Glu Leu Ser Ile
  -40 -35 -30 -25
- Glu Asn Trp Ile Met Pro Ala Val Tyr Ala Gly His Phe Ser His Val
  -20 -15 -10
- Val Trp Phe His Pro Thr Trp Ala Gln Gln Ile Arg Glu Gly Arg His
  -5 1 5

His Phe

- (2) INFORMATION FOR SEQ ID NO: 313:
  - (i) SEQUENCE CHARACTERISTICS:
    - (A) LENGTH: 109 amino acids
    - (B) TYPE: AMINO ACID
    - (D) TOPOLOGY: LINEAR
  - (ii) MOLECULE TYPE: PROTEIN
  - (vi) ORIGINAL SOURCE:
    - (A) ORGANISM: Homo Sapiens
    - (F) TISSUE TYPE: Brain

(ix) FEATURE:

(A) NAME/KEY: sig\_peptide

(B) LOCATION: -47..-1

- (C) IDENTIFICATION METHOD: Von Heijne matrix
- (D) OTHER INFORMATION: score 6.3

seq SSCVLLTALVALA/AY

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 313:

Met Ser Ser Cys Arg Gly Gln Lys Val Ala Gly Gly Leu Arg Val Val -45 -40 -35

Ser Pro Phe Pro Leu Cys Gln Pro Ala Gly Glu Pro Ser Arg Gly Lys
-30 -25 -20

Met Arg Ser Ser Cys Val Leu Leu Thr Ala Leu Val Ala Leu Ala Ala -15 -5 1

Tyr Tyr Val Tyr Ile Pro Leu Pro Gly Ser Val Ser Asp Pro Trp Lys  $\frac{10}{10}$ 

Leu Met Leu Leu Asp Ala Thr Phe Arg Gly Ala Xaa Xaa Xaa Ser Xaa 20 25 30

Leu Val Xaa Tyr Leu Gly Leu Ser Xaa His Leu Leu Ala Leu Xaa Xaa 35 40 45

Xaa Leu Phe Leu Leu Ala Lys Lys Ala Arg Gly Leu Leu 50 55 60

- (2) INFORMATION FOR SEQ ID NO: 314:
  - (i) SEQUENCE CHARACTERISTICS:
    - (A) LENGTH: 72 amino acids
    - (B) TYPE: AMINO ACID
    - (D) TOPOLOGY: LINEAR
  - (ii) MOLECULE TYPE: PROTEIN
  - (vi) ORIGINAL SOURCE:
    - (A) ORGANISM: Homo Sapiens
    - (F) TISSUE TYPE: Brain
  - (ix) FEATURE:
    - (A) NAME/KEY: sig\_peptide
    - (B) LOCATION: -42..-1
    - (C) IDENTIFICATION METHOD: Von Heijne matrix
    - (D) OTHER INFORMATION: score 6.1

seq DLAVALSLLPAWT/ES

- (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 314:
- Mot Ile Ile Pro Phe Lys Ile Lys Asn Leu Gly Gly Arg Val Leu Leu -40 -35 -30
- Ser Gly Arg Glu Met Phe Pro Ala Ser Val Arg Ala Pro Asp Leu Ala

**-25 -20 -15** 

Val Ala Leu Ser Leu Leu Pro Ala Trp Thr Glu Ser Pro Thr Arg Gly
-10 -5 1 5

Ser His Gln Ser Gln Ala Arg Ala His Ser Arg Ala Leu Arg Lys Gln
10 15 20

Ser Arg Asn Thr Arg Ser Pro Arg 25 30

- (2) INFORMATION FOR SEQ ID NO: 315:
  - (i) SEQUENCE CHARACTERISTICS:
    - (A) LENGTH: 60 amino acids
    - (B) TYPE: AMINO ACID
    - (D) TOPOLOGY: LINEAR
  - (ii) MOLECULE TYPE: PROTEIN
  - (vi) ORIGINAL SOURCE:
    - (A) ORGANISM: Homo Sapiens
    - (F) TISSUE TYPE: Brain
  - (ix) FEATURE:
    - (A) NAME/KEY: sig\_peptide
    - (B) LOCATION: -53..-1
    - (C) IDENTIFICATION METHOD: Von Heijne matrix
    - (D) OTHER INFORMATION: score 6

seq ALILLLAQKGPS/XF

- (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 315:
- Met Val Cys Ser Ala Pro Arg Lys Ile Val Val Arg Ala Phe Ile Thr
  -50 -45 -40
- Ile Ile Phe Ile Tyr Tyr Ala Ile Lys Lys Arg Ala Asn Glu Pro Ala -35 -30 -25
- Ala Tyr Leu Met Leu Lys Pro Glu Ala Leu Ile Leu Leu Leu Ala
  -20 -15 -10
- Gln Lys Gly Pro Ser Xaa Phe Leu Leu Val Trp Arg
  -5 5
- (2) INFORMATION FOR SEQ ID NO: 316:
  - (i) SEQUENCE CHARACTERISTICS:
    - (A) LENGTH: 60 amino acids
    - (B) TYPE: AMINO ACID
    - (D) TOPOLOGY: LINEAR
  - (ii) MOLECULE TYPE: PROTEIN
  - (vi) ORIGINAL SOURCE:
    - (A) ORGANISM: Homo Sapiens

(F) TISSUE TYPE: Brain

(ix) FEATURE:

- (A) NAME/KEY: sig\_peptide
- (B) LOCATION: -40..-1
- (C) IDENTIFICATION METHOD: Von Heijne matrix
- (D) OTHER INFORMATION: score 5.9

seq VCSALCSLGEVRP/XE

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 316:

Met Thr Glu Ser Ser Met Lys Lys Leu Ala Ser Thr Leu Leu Asp Ala

Ile Thr Asp Lys Asp Pro Leu Val Gln Glu Gln Val Cys Ser Ala Leu -10

Cys Ser Leu Gly Glu Val Arg Pro Xaa Glu Thr Leu Arg Ala Cys Glu

Glu Tyr Leu Arg Xaa Met Thr Ser Trp His Thr Arg 15

- (2) INFORMATION FOR SEQ ID NO: 317:
  - (i) SEQUENCE CHARACTERISTICS:
    - (A) LENGTH: 59 amino acids
    - (B) TYPE: AMINO ACID
    - (D) TOPOLOGY: LINEAR
  - (ii) MOLECULE TYPE: PROTEIN
  - (vi) ORIGINAL SOURCE:
    - (A) ORGANISM: Homo Sapiens
    - (F) TISSUE TYPE: Brain
  - (ix) FEATURE:
    - (A) NAME/KEY: sig\_peptide
    - (B) LOCATION: -43...1
    - (C) IDENTIFICATION METHOD: Von Heijne matrix
    - (D) OTHER INFORMATION: score 5.9

seq VFLFHCTSGLSSC/KC

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 317:

Met Gln Glu Thr Asp Cys Asn Lys Arg Trp Gly Arg Gly Leu Gly Gly

Leu Trp Ser Glu Thr Gly Arg Arg Phe His Cys Lys Ser Phe Val Phe

Led Phe His Cys Thr Ser Gly Leu Ser Ser Cys Lys Cys Ser Lys Lys

His Xaa Lys Tyr Cys Phe Cys Phe Val Ala Ser

Ser Pro Ala Phe Leu Ala Val Ala Gly Pro Gly Trp Ala Arg Pro Gly
-10 -5

Cys Xaa Leu Arg Thr Lys Tyr Asp Ser Gln Leu Ala Arg His Leu Leu 5 10

Gln Pro Gln Phe Pro Gly Leu Thr Leu Gly Thr Leu Val Gln Pro Ala 20 25 30 35

His Trp Gly Met Gly Gly Gly Thr Gly Gly Val Leu Gly Glu Gly Gly 40 45 50

Gly His Ser Tyr Ala Glu His Gly Thr Cys Leu Gln Ser Cys Ser Thr 60 65

Asp Val Leu Xaa His Val Leu Leu Ala
70 75

## (2) INFORMATION FOR SEQ ID NO: 320:

- (i) SEQUENCE CHARACTERISTICS:
  - (A) LENGTH: 125 amino acids
  - (B) TYPE: AMINO ACID
  - (D) TOPOLOGY: LINEAR
- (ii) MOLECULE TYPE: PROTEIN
- (vi) ORIGINAL SOURCE:
  - (A) ORGANISM: Homo Sapiens
  - (F) TISSUE TYPE: Brain
- (ix) FEATURE:
  - (A) NAME/KEY: sig\_peptide
  - (B) LOCATION: -18..-1
  - (C) IDENTIFICATION METHOD: Von Heijne matrix
  - (D) OTHER INFORMATION: score 5.6

seq WHFLASFFPRAGC/HG

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 320:

Met Leu Gln Met Leu Trp His Phe Leu Ala Ser Phe Phe Pro Arg Ala

Gly Cys His Gly Ser Arg Glu Gly Asp Asp Arg Glu Val Arg Gly Thr

Pro Ala Pro Ala Trp Arg Asp Gln Met Ala Ser Phe Leu Gly Lys Gln 15 20 25 30

Asp Gly Arg Ala Glu Ala Thr Glu Lys Arg Pro Thr Ile Leu Leu Val 35 40 45

Val Gly Pro Ala Glu Gln Phe Pro Lys Lys Ile Val Gln Ala Gly Asp

Lys Asp Leu Asp Gly Gln Leu Asp Phe Glu Glu Phe Val His Tyr Leu
70

WO 99/06552 PCT/IB98/01236 322

```
(2) INFORMATION FOR SEQ ID NO: 318:
```

- (i) SEQUENCE CHARACTERISTICS:
  - (A) LENGTH: 45 amino acids
  - (B) TYPE: AMINO ACID
  - (D) TOPOLOGY: LINEAR
- (ii) MOLECULE TYPE: PROTEIN
- (vi) ORIGINAL SOURCE:
  - (A) ORGANISM: Homo Sapiens
  - (F) TISSUE TYPE: Brain
- (ix) FEATURE:
  - (A) NAME/KEY: sig\_peptide
  - (B) LOCATION: -17..-1
  - (C) IDENTIFICATION METHOD: Von Heijne matrix
  - (D) OTHER INFORMATION: score 5.8

seq VPWLSSTVSCAQG/LR

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 318:

Met Leu Leu Glu Val Pro Trp Leu Ser Ser Thr Val Ser Cys Ala Gln -10

Gly Leu Arg Leu Ala Gln His Arg Val Pro Phe Phe Tyr Ser Asn Val 5

Ser Leu Cys Lys Leu Leu Leu Pro Ala Xaa Leu His Gly 20

- (2) INFORMATION FOR SEQ ID NO: 319:
  - (i) SEQUENCE CHARACTERISTICS:
    - (A) LENGTH: 105 amino acids
    - (B) TYPE: AMINO ACID
    - (D) TOPOLOGY: LINEAR
  - (ii) MOLECULE TYPE: PROTEIN
  - (vi) ORIGINAL SOURCE:
    - (A) ORGANISM: Homo Sapiens
    - (F) TISSUE TYPE: Brain
  - (ix) FEATURE:
    - (A) NAME/KEY: sig\_peptide
    - (B) LOCATION: -29..-1
    - (C) IDENTIFICATION METHOD: Von Heijne matrix
    - (D) OTHER INFORMATION: score 5.7

seq SPAFLAVAGPGWA/RP

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 319:

Met Ser Gly Gly Arg Met Gln Ala Arg Cys Ser Gln Gln Ser Thr Trp

Gln Asp His Glu Lys Lys Leu Arg Leu Val Phe Lys Ser Leu Asp Lys 80 90

Lys Asn Asp Gly Arg Ile Asp Ala Gln Glu Ile Met Gln 95 100 105

- (2) INFORMATION FOR SEQ ID NO: 321:
  - (i) SEQUENCE CHARACTERISTICS:
    - (A) LENGTH: 37 amino acids
    - (B) TYPE: AMINO ACID
    - (D) TOPOLOGY: LINEAR
  - (ii) MOLECULE TYPE: PROTEIN
  - (vi) ORIGINAL SOURCE:
    - (A) ORGANISM: Homo Sapiens
    - (F) TISSUE TYPE: Brain
  - (ix) FEATURE:
    - (A) NAME/KEY: sig\_peptide
    - (B) LOCATION: -20..-1
    - (C) IDENTIFICATION METHOD: Von Heijne matrix
    - (D) OTHER INFORMATION: score 5.6

seq SLVCLLAMGKGLG/SS

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 321:

Met Tyr Ser His Pro Val Ser Ser Leu Val Cys Leu Leu Ala Met Gly -20 -15 -10 -5

Lys Gly Leu Gly Ser Ser Gln Ala Leu Val Gln Pro Asp Thr Trp Pro 1 5 10

His Thr Ser Pro Arg

- (2) INFORMATION FOR SEQ ID NO: 322:
  - (i) SEQUENCE CHARACTERISTICS:
    - (A) LENGTH: 92 amino acids
    - (B) TYPE: AMINO ACID
    - (D) TOPOLOGY: LINEAR
  - (ii) MOLECULE TYPE: PROTEIN
  - (vi) ORIGINAL SOURCE:
    - (A) ORGANISM: Homo Sapiens
    - (F) TISSUE TYPE: Brain
  - (ix) FEATURE:
    - (A) NAME/KEY: sig\_peptide
    - (B) LOCATION: -35..-1
    - (C) IDENTIFICATION METHOD: Von Heijne matrix
    - (D) OTHER INFORMATION: score 5.6

seq FIFMEVLGSGAFS/EV

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 322:

Met Gly Arg Lys Glu Glu Asp Asp Cys Ser Xaa Trp Lys Lys Gln Thr -35 -25 -25

Thr Asn Ile Arg Lys Thr Phe Ile Phe Met Glu Val Leu Gly Ser Gly -15 -10 -5

Ala Phe Ser Glu Val Phe Leu Val Lys Gln Arg Leu Thr Gly Lys Leu  $1 \hspace{1cm} 5 \hspace{1cm} 10$ 

Phe Ala Leu Lys Cys Ile Lys Lys Ser Pro Ala Phe Arg Asp Ser Ser 15 20 25

Leu Glu Asn Glu Ile Ala Val Leu Lys Lys Ile Lys His Glu Asn Ile 30 45

Val Thr Leu Glu Asp Ile Tyr Glu Ser Thr Gln Gly
50 55

- (2) INFORMATION FOR SEQ ID NO: 323:
  - (i) SEQUENCE CHARACTERISTICS:
    - (A) LENGTH: 48 amino acids
    - (B) TYPE: AMINO ACID
    - (D) TOPOLOGY: LINEAR
  - (ii) MOLECULE TYPE: PROTEIN
  - (vi) ORIGINAL SOURCE:
    - (A) ORGANISM: Homo Sapiens
    - (F) TISSUE TYPE: Brain
  - (ix) FEATURE:
    - (A) NAME/KEY: sig\_peptide
    - (B) LOCATION: -29..-1
    - (C) IDENTIFICATION METHOD: Von Heijne matrix
    - (D) OTHER INFORMATION: score 5.6

seq LLPNQSLFSLARA/VR

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 323:

Met Met 11e Ala Val Phe Gly Asn Ala Asn Asp Arg Asn Val Leu Thr -25 -20 -15

Leu Leu Pro Asn Gln Ser Leu Phe Ser Leu Ala Arg Ala Val Arg Asn
-10 -5

His Leu Leu Glu Glu Arg Arg Leu Thr Thr Tyr Gly Val Leu Cys 5 10

(2) INFORMATION FOR SEO ID NO: 324:

WO 99/06552 326

- (i) SEQUENCE CHARACTERISTICS:
  - (A) LENGTH: 58 amino acids
  - (B) TYPE: AMINO ACID
  - (D) TOPOLOGY: LINEAR
- (ii) MOLECULE TYPE: PROTEIN
- (vi) ORIGINAL SOURCE:
  - (A) ORGANISM: Homo Sapiens
  - (F) TISSUE TYPE: Brain
- (ix) FEATURE:
  - (A) NAME/KEY: sig\_peptide
  - (B) LOCATION: -19..-1
  - (C) IDENTIFICATION METHOD: Von Heijne matrix
  - (D) OTHER INFORMATION: score 5.6 seq LVVTAWFFGMCRS/KA
- (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 324:

Met Phe Phe Glu Leu Pro Leu Val Val Thr Ala Trp Phe Phe Gly Met -15 -10 -5

Cys Arg Ser Lys Ala Leu Leu Gly Asn Ala Arg Ser Ala Leu Cys Leu 1 5 10

Gln Thr Lys Ala Cys Ala Ser Ser Thr Gln Pro Asp Thr His Asn Glu
15 20 25

His His Pro Arg Asn Pro Cys Pro Tyr Leu

- (2) INFORMATION FOR SEQ ID NO: 325:
  - (i) SEQUENCE CHARACTERISTICS:
    - (A) LENGTH: 54 amino acids
    - (B) TYPE: AMINO ACID
    - (D) TOPOLOGY: LINEAR
  - (ii) MOLECULE TYPE: PROTEIN
  - (vi) ORIGINAL SOURCE:
    - (A) ORGANISM: Homo Sapiens
    - (F) TISSUE TYPE: Brain
  - (ix) FEATURE:
    - (A) NAME/KEY: sig\_peptide
    - (B) LOCATION: -44..-1
    - (C) IDENTIFICATION METHOD: Von Heijne matrix
    - (D) OTHER INFORMATION: score 5.5

seq FLLIVANVHFSQT/WV

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 325:

Met Asn His Asn Ile Ile Ile Cys Val Met Tyr Ile Val Pro Phe Leu
-40 -35 -30

Met Thr Lys Cys Leu Tyr Phe Cys His Ser Cys Lys Arg Gly Ser Phe +25 +20 -15

Leu Leu Ile Val Ala Asn Val His Phe Ser Gln Thr Trp Val Phe Ser

Gly Lys Pro Tyr Lys Gly
5

- (2) INFORMATION FOR SEQ ID NO: 326:
  - (i) SEQUENCE CHARACTERISTICS:
    - (A) LENGTH: 53 amino acids
    - (B) TYPE: AMINO ACID
    - (D) TOPOLOGY: LINEAR
  - (ii) MOLECULE TYPE: PROTEIN
  - (vi) ORIGINAL SOURCE:
    - (A) ORGANISM: Homo Sapiens
    - (F) TISSUE TYPE: Brain
  - (ix) FEATURE:
    - (A) NAME/KEY: sig\_peptide
    - (B) LOCATION: -21..-1
    - (C) IDENTIFICATION METHOD: Von Heijne matrix
    - (D) OTHER INFORMATION: score 5.5 seq LTGLCXCCLQALG/LA
      - •
  - (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 326:

Met Ser Cys Gly Ser Ala Ala Ser Leu Thr Gly Leu Cys Xaa Cys Cys -20 -15 -10

Leu Gln Ala Leu Gly Leu Ala Trp Arg Arg Gly Leu Thr Gly Pro
-5 5 10

Gly Leu Pro Pro Val Leu Gln Ile Cys Cys Pro Arg Ser Leu Arg Gly
15 20 25

Val Thr Ala Pro Thr 30

- (2) INFORMATION FOR SEQ ID NO: 327:
  - (i) SEQUENCE CHARACTERISTICS:
    - (A) LENGTH: 68 amino acids
    - (B) TYPE: AMINO ACID
      (D) TOPOLOGY: LINEAR
  - (:1) MOLECULE TYPE: PROTEIN
  - (vi) ORIGINAL SOURCE:
    - (A) ORGANISM: Homo Sapiens
    - (F) TISSUE TYPE: Brain

- (ix) FEATURE:
  - (A) NAME/KEY: sig\_peptide
  - (B) LOCATION: -46..-1
  - (C) IDENTIFICATION METHOD: Von Heijne matrix
  - (D) OTHER INFORMATION: score 5.4 seq VLFFVGLITNGLA/MR
- (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 327:

Met Gln Ala Val Asp Asn Leu Thr Ser Ala Pro Gly Asn Thr Ser Leu
-45 -35

Cys Thr Arg Asp Tyr Lys Ile Thr Gln Val Leu Phe Pro Leu Leu Tyr
-30 -25 -20 -15

Thr Val Leu Phe Phe Val Gly Leu Ile Thr Asn Gly Leu Ala Met Arg
-10 -5 1

Ile Phe Phe Gln Ile Arg Ser Lys Ser Asn Phe Ile Ile Phe Leu Lys
5 10 15

Asn Thr Val Lys

- (2) INFÓRMATION FOR SEQ ID NO: 328:
  - (i) SEQUENCE CHARACTERISTICS:
    - (A) LENGTH: 28 amino acids
    - (B) TYPE: AMINO ACID
    - (D) TOPOLOGY: LINEAR
  - (ii) MOLECULE TYPE: PROTEIN
  - (vi) ORIGINAL SOURCE:
    - (A) ORGANISM: Homo Sapiens
      - (F) TISSUE TYPE: Brain
  - (ix) FEATURE:
    - (A) NAME/KEY: sig\_peptide
      - (B) LOCATION: -20..-1
      - (C) IDENTIFICATION METHOD: Von Heijne matrix
      - (D) OTHER INFORMATION: score 5.3

seq LCSSCCSWGPAAG/AL

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 328:

Met Ala Ala Ala Met Xaa Leu Leu Cys Ser Ser Cys Cys Ser Trp Gly
-20 -15 -10 -5

Pro Ala Ala Gly Ala Leu Gln Asn Pro Gln Arg Gly

- (2) INFORMATION FOR SEQ ID NO: 329:
  - (1) SEQUENCE CHARACTERISTICS:

PCT/IB98/01236 329

(A) LENGTH: 30 amino acids

(B) TYPE: AMINO ACID (D) TOPOLOGY: LINEAR

- (ii) MOLECULE TYPE: PROTEIN
- (vi) ORIGINAL SOURCE:
  - (A) ORGANISM: Homo Sapiens
  - (F) TISSUE TYPE: Brain
- (ix) FEATURE:
  - (A) NAME/KEY: sig\_peptide
  - (B) LOCATION: -25..-1
  - (C) IDENTIFICATION METHOD: Von Heijne matrix
  - (D) OTHER INFORMATION: score 5.3

seq SVVKVLSLRKAQA/QS

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 329:

Met Asp Phe Ile Lys Asp Gln Ser Leu Ser His Arg Ser Val Val Lys -15

Val Leu Ser Leu Arg Lys Ala Gln Ala Gln Ser Ile Leu Glu -- 5

- (2) INFORMATION FOR SEQ ID NO: 330:
  - (i) SEQUENCE CHARACTERISTICS:
    - (A) LENGTH: 75 amino acids
    - (B) TYPE: AMINO ACID
    - (D) TOPOLOGY: LINEAR
  - (ii) MOLECULE TYPE: PROTEIN
  - (vi) ORIGINAL SOURCE:
    - (A) ORGANISM: Homo Sapiens
    - (F) TISSUE TYPE: Brain
  - (ix) FEATURE:
    - (A) NAME/KEY: sig\_peptide
    - (B) LOCATION: -28..-1
    - (C) IDENTIFICATION METHOD: Von Heijne matrix
    - (D) OTHER INFORMATION: score 5.3

seq RISCAFSLASSTA/RQ

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 330:

Met Thr Arg Pro Phe Trp Ala Ser Cys Ser Thr Trp Ala Thr Ser Arg

Ile Ser Cys Ala Phe Ser Leu Ala Ser Ser Thr Ala Arg Gln Thr Ser

The Ala Cys Cys Ala Thr His Arg Thr Ala Trp Ala Ser Arg Pro Gly 15

Pro Ary Arg Pro Trp Cys Cys Arg Tyr Ser Lys Pro Leu Thr Thr Trp

25 30 35

Pro Val Arg Met Met Arg Arg Glu Gly Ser Xaa 40 45

- (2) INFORMATION FOR SEQ ID NO: 331:
  - (i) SEQUENCE CHARACTERISTICS:
    - (A) LENGTH: 35 amino acids
    - (B) TYPE: AMINO ACID
    - (D) TOPOLOGY: LINEAR
  - (ii) MOLECULE TYPE: PROTEIN
  - (vi) ORIGINAL SOURCE:
    - (A) ORGANISM: Homo Sapiens
    - (F) TISSUE TYPE: Brain
  - (ix) FEATURE:
    - (A) NAME/KEY: sig\_peptide
    - (B) LOCATION: -16..-1
    - (C) IDENTIFICATION METHOD: Von Heijne matrix
    - (D) OTHER INFORMATION: score 5.3

seq CAVSLTTAAVAFG/DE

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 331:

Met Lys Ser Cys Ala Val Ser Leu Thr Thr Ala Ala Val Ala Phe Gly
-15 -5

Asp Glu Ala Lys Lys Met Ala Glu Gly Lys Ala Ser Arg Glu Ser Glu  $1 \hspace{1cm} 5 \hspace{1cm} 10 \hspace{1cm} 15$ 

Glu Glu Thr

- (2) INFORMATION FOR SEQ ID NO: 332:
  - (i) SEQUENCE CHARACTERISTICS:
    - (A) LENGTH: 39 amino acids
    - (B) TYPE: AMINO ACID
    - (D) TOPOLOGY: LINEAR
  - (ii) MOLECULE TYPE: PROTEIN
  - (vi) ORIGINAL SOURCE:
    - (A) ORGANISM: Homo Sapiens
    - (F) TISSUE TYPE: Brain
  - (ix) FEATURE:
    - (A) NAME/KEY: sig\_peptide
    - (B) LOCATION: -21..-1
    - (C) IDENTIFICATION METHOD: Von Heijne matrix
    - (D) OTHER INFORMATION: score 5.2 seq LSLSLICLRMSLS/LY
  - (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 332:

Met Ser Ile His Glu Cys Ala Cys Leu Ser Leu Ser Leu Ile Cys Leu -20 -15

Arg Met Ser Leu Ser Leu Tyr Pro Pro Pro Ala Ser Met Ile Leu Leu

Pro Gln Thr Trp Lys Pro Arg 15

- (2) INFORMATION FOR SEQ ID NO: 333:
  - (i) SEQUENCE CHARACTERISTICS:
    - (A) LENGTH: 42 amino acids
    - (B) TYPE: AMINO ACID
    - (D) TOPOLOGY: LINEAR
  - (ii) MOLECULE TYPE: PROTEIN
  - (vi) ORIGINAL SOURCE:
    - (A) ORGANISM: Homo Sapiens
    - (F) TISSUE TYPE: Brain
  - (ix) FEATURE:
    - (A) NAME/KEY: sig\_peptide
    - (B) LOCATION: -15..-1
    - (C) IDENTIFICATION METHOD: Von Heijne matrix
    - (D) OTHER INFORMATION: score 5.2

seq SGLSFLSVFSLWC/EP

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 333:

Met Leu Ser Gly Leu Ser Phe Leu Ser Val Phe Ser Leu Trp Cys Glu

Pro Thr Leu Pro Ala Leu Gly Asn Gly Ser Val Leu Gly Val Arg Xaa 1.0

Ser Ser Ser Ser Ala Gln Cys Ser Leu 20

- (2) INFORMATION FOR SEQ ID NO: 334:
  - (i) SEQUENCE CHARACTERISTICS:
    - (A) LENGTH: 87 amino acids
    - (B) TYPE: AMINO ACID
    - (D) TOPOLOGY: LINEAR
  - (ii) MOLECULE TYPE: PROTEIN
  - (vi) ORIGINAL SOURCE:
    - (A) ORGANISM: Homo Sapiens
    - (F) TISSUE TYPE: Brain
  - (ix) FEATURE:

- (A) NAME/KEY: sig peptide
- (B) LOCATION: -85..-1
- (C) IDENTIFICATION METHOD: Von Heijne matrix
- (D) OTHER INFORMATION: score 5.2

seq LYSILHFPFWVHG/RX

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 334:

Met Gly Leu Lys Asp Lys Ser Gln Ala Pro Ala Ser Gly Leu Gly Val -85 -75 -70

Leu Arg Gly Gln Arg Ser Gly Ser Phe Ile Ser Met Pro Ala Pro Ala -65 -60 -55

Ser Gly Gln Xaa Pro Glu Glu Ser Arg Ser Pro Ala Pro Pro Val Ala
-50
-45
-40

Ser Arg Ser Gln Asn Arg Gly Tyr Arg Pro Trp His Gly Pro Leu Trp
-35
-30
-25

Val His Gln Ser Val Arg Phe Gly Leu Tyr Ser Ile Leu His Phe Pro
-20 -15 -10

Phe Trp Val His Gly Arg Xaa -5

- (2) INFORMATION FOR SEQ ID NO: 335:
  - (i) SEQUENCE CHARACTERISTICS:
    - (A) LENGTH: 67 amino acids
    - (B) TYPE: AMINO ACID
    - (D) TOPOLOGY: LINEAR
  - (ii) MOLECULE TYPE: PROTEIN
  - (vi) ORIGINAL SOURCE:
    - (A) ORGANISM: Homo Sapiens
    - (F) TISSUE TYPE: Brain
  - (ix) FEATURE:
    - (A) NAME/KEY: sig\_peptide
    - (B) LOCATION: -43..-1
    - (C) IDENTIFICATION METHOD: Von Heijne matrix
    - (D) OTHER INFORMATION: score 5.2

seq PMQLLQVLSDVLA/EI

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 335:

Met Ser Asp Gln Ile Lys Phe Ile Met Asp Ser Leu Asn Lys Glu Pro

Phe Arg Lys Asn Tyr Asn Leu Ile Thr Phe Asp Ser Leu Glu Pro Met
-25 -20 -15

Gln Leu Leu Gln Val Leu Ser Asp Val Leu Ala Glu Ile Asp Pro Lys
-10 -5 1 5

Val Arg Val Phe Ser Phe Phe Leu Met Gly Ser Arg Lys Pro Ile Ser

Pro Ser Trp

- (2) INFORMATION FOR SEQ ID NO: 336:
  - (i) SEQUENCE CHARACTERISTICS:
    - (A) LENGTH: 110 amino acids
    - (B) TYPE: AMINO ACID
    - (D) TOPOLOGY: LINEAR
  - (ii) MOLECULE TYPE: PROTEIN
  - (vi) ORIGINAL SOURCE:
    - (A) ORGANISM: Homo Sapiens
    - (F) TISSUE TYPE: Brain
  - (ix) FEATURE:
    - (A) NAME/KEY: sig\_peptide
    - (B) LOCATION:  $-10\overline{4}..-1$
    - (C) IDENTIFICATION METHOD: Von Heijne matrix
    - (D) OTHER INFORMATION: score 5.1

seq SSVASLTATPSLA/SP

- (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 336:
- Met Ser Pro Ser Cys Leu His Pro Asp Leu Trp Ser Met Cys Leu Glu
- Val Pro Ser Phe Thr Ala Thr Asp Ser Val Asn Cys Gly Cys Cys Leu
  -85 -80 -75
- Glu Leu Ala Thr Glu Pro Ala Arg Asn Ile Arg Ser Thr Thr Arg Ala
  -70
  -65
  -60
- Ser Leu Leu Arg Cys Ser Ser Phe Thr Ser Thr Arg Asn Ser Thr Gly
  -55 -50 -45
- Ile Ser Ala Leu Pro Pro Ala Ala Pro Met Ala Trp Pro Phe Ser Ala -40 -35 -30 -25
- Ser Leu Ser Thr Leu Pro Val Pro Leu Thr His Ser Ser Val Ala Ser -20 -15 -10
- Leu Thr Ala Thr Pro Ser Leu Ala Ser Pro Thr Arg Met Met
- (2) INFORMATION FOR SEQ ID NO: 337:
  - (i) SEQUENCE CHARACTERISTICS:
    - (A) LENGTH: 24 amino acids
    - (B) TYPE: AMINO ACID
    - (D) TOPOLOGY: LINEAR
  - (ii) MOLECULE TYPE: PROTEIN

- (vi) ORIGINAL SOURCE:
  - (A) ORGANISM: Homo Sapiens
  - (F) TISSUE TYPE: Brain
- (ix) FEATURE:
  - (A) NAME/KEY: sig\_peptide
  - (B) LOCATION: -16..-1
  - (C) IDENTIFICATION METHOD: Von Heijne matrix
  - (D) OTHER INFORMATION: score 5.1

seq SFHLLLDPSSTQS/SI

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 337:

Met Asp Leu Ser Phe His Leu Leu Leu Asp Pro Ser Ser Thr Gln Ser -15 -10

Ser Ile Leu Lys His Leu Pro Cys

- (2) INFORMATION FOR SEQ ID NO: 338:
  - (i) SEQUENCE CHARACTERISTICS:
    - (A) LENGTH: 53 amino acids
      - (B) TYPE: AMINO ACID
      - (D) TOPOLOGY: LINEAR
  - (ii) MOLECULE TYPE: PROTEIN
  - (vi) ORIGINAL SOURCE:
    - (A) ORGANISM: Homo Sapiens
    - (F) TISSUE TYPE: Brain
  - (ix) FEATURE:
    - (A) NAME/KEY: sig\_peptide
    - (B) LOCATION: -26..-1
    - (C) IDENTIFICATION METHOD: Von Heijne matrix
    - (D) OTHER INFORMATION: score 5

seq VISVLILVGFGAC/IY

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 338:

Met Pro His Phe Leu Asp Trp Phe Val Xaa Val Tyr Leu Val Ile Ser
-25 -20 -15

Val Leu Ile Leu Val Gly Phe Gly Ala Cys Ile Tyr Tyr Phe Glu Pro -10 -5 5

Gly Leu Gln Glu Ala His Lys Trp Arg Met Xaa Arg Pro Trp Thr

Ala Thr Ser Thr Gly 25

(2) INFORMATION FOR SEQ ID NO: 339:

(1) SEQUENCE CHARACTERISTICS: (A) LENGTH: 39 amino acids (B) TYPE: AMINO ACID (D) TOPOLOGY: LINEAR (ii) MOLECULE TYPE: PROTEIN (vi) ORIGINAL SOURCE: (A) ORGANISM: Homo Sapiens (F) TISSUE TYPE: Brain (ix) FEATURE: (A) NAME/KEY: sig\_peptide (B) LOCATION: -30..-1 (C) IDENTIFICATION METHOD: Von Heijne matrix (D) OTHER INFORMATION: score 5 seq IVGLLAQLEKINA/EP (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 339: Met Ser Lys Leu Lys Val Ile Pro Glu Lys Ser Leu Thr Asn Asn Ser -30 -25 -20 Arg Ile Val Gly Leu Leu Ala Gln Leu Glu Lys Ile Asn Ala Glu Pro -10 Ser Glu Ser Asp Thr Ser Arg (2) INFORMATION FOR SEQ ID NO: 340: (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 43 amino acids (B) TYPE: AMINO ACID (D) TOPOLOGY: LINEAR (ii) MOLECULE TYPE: PROTEIN (vi) ORIGINAL SOURCE: (A) ORGANISM: Homo Sapiens (F) TISSUE TYPE: Brain (ix) FEATURE: (A) NAME/KEY: sig\_peptide (B) LOCATION: -23..-1 (C) IDENTIFICATION METHOD: Von Heijne matrix (D) OTHER INFORMATION: score 5 seq LIPAMAFLSCVRP/ES (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 340: Mat Met Ser Ala Ser Arg Leu Ala Gly Thr Leu Ile Pro Ala Met Ala

Phe Leu Ser Cys Val Arg Pro Glu Ser Xaa Glu Pro Cys Val Glu Val

Val Pro Asn Ile Thr Tyr Gln Cys Met Glu Leu 10 15 20

- (2) INFORMATION FOR SEQ ID NO: 341:
  - (i) SEQUENCE CHARACTERISTICS:
    - (A) LENGTH: 65 amino acids
    - (B) TYPE: AMINO ACID
    - (D) TOPOLOGY: LINEAR
  - (ii) MOLECULE TYPE: PROTEIN
  - (vi) ORIGINAL SOURCE:
    - (A) ORGANISM: Homo Sapiens
    - (F) TISSUE TYPE: Brain
  - (ix) FEATURE:
    - (A) NAME/KEY: sig\_peptide
    - (B) LOCATION: -49..-1
    - (C) IDENTIFICATION METHOD: Von Heijne matrix
    - (D) OTHER INFORMATION: score 4.9

seq VTVCCXLVAFLFC/IL

- (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 341:
- Met Val Asp Gly Thr Gln Leu Arg Gly Leu Thr Arg Met Tyr Gln Val
  -45 -40 -35
- Pro Leu Xaa Leu Asp Arg Asp Glu Thr Leu Val Arg Leu Arg Phe Thr
  -30
  -25
  -20
- Met Val Ala Leu Val Thr Val Cys Cys Xaa Leu Val Ala Phe Leu Phe
  -15 -10 -5
- Cys Ile Leu Trp Ser Leu Leu Phe His Phe Lys Glu Thr Thr Ala Thr
  1 5 10 15

Gly

- (2) INFORMATION FOR SEO ID NO: 342:
  - (i) SEQUENCE CHARACTERISTICS:
    - (A) LENGTH: 34 amino acids
    - (3) TYPE: AMINO ACID
    - (D) TOPOLOGY: LINEAR
  - (ii) MOLECULE TYPE: PROTEIN
  - (vi) ORIGINAL SOURCE:
    - (A) ORGANISM: Homo Sapiens
    - (F) TISSUE TYPE: Brain
  - (ix) FEATURE:
    - (A) NAME/KEY: sig\_peptide
    - [3] LOCATION: -26..-1

(C) IDENTIFICATION METHOD: Von Heijne matrix

- (b) OTHER INFORMATION: score 4.9
  seq LISMLQMLAVIIT/NT
- (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 342:

Met Lys Gln Asn Phe Leu Val Leu Asn Ser Val Trp Tyr Leu Ile Ser

Met Leu Gln Met Leu Ala Val Ile Ile Thr Asn Thr Thr Ile Thr Thr -10 -5 1

Ile Gly

- (2) INFORMATION FOR SEQ ID NO: 343:
  - (i) SEQUENCE CHARACTERISTICS:
    - (A) LENGTH: 124 amino acids
    - (B) TYPE: AMINO ACID
    - (D) TOPOLOGY: LINEAR
  - (ii) MOLECULE TYPE: PROTEIN
  - (vi) ORIGINAL SOURCE:
    - (A) ORGANISM: Homo Sapiens
    - (F) TISSUE TYPE: Brain
  - (ix) FEATURE:
    - (A) NAME/KEY: sig\_peptide
    - (B) LOCATION: -59..-1
    - (C) IDENTIFICATION METHOD: Von Heijne matrix
    - (D) OTHER INFORMATION: score 4.9 seq LVEMCLEVLGSSA/GD
  - (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 343:

Met Glu Cys Gln Asn Ser Ser Leu Lys Lys Cys Leu Leu Val Glu Lys
-55 -50 -45

Ser Leu Val Lys Ala Ser Tyr Leu Ile Ala Phe Gln Thr Ala Ala Ser -40 -35 -30

Lys Lys Pro Phe Ser Ile Ala Glu Glu Leu Ile Lys Pro Tyr Leu Val

Glu Met Cys Leu Glu Val Leu Gly Ser Ser Ala Gly Asp Lys Met Lys -10 -5 1 5

Thr Ile Pro Leu Ser Asn Val Thr Ile Gln His Arg Ile Asp Glu Leu 10 15 20

Ser Ala Asp Ile Glu Asp Gln Leu Ile Gln Lys Val Arg Glu Ser Lys 25 30 35

Trp Phe Ala Leu Gln Ile Asp Glu Ser Ser Glu Ile Ser Asn Ile Thr 40 45 50

Leu Leu Cys Tyr Ile Arg Phe Ile Asp Tyr Asp 55 60 65

- (2) INFORMATION FOR SEQ ID NO: 344:
  - (i) SEQUENCE CHARACTERISTICS:
    - (A) LENGTH: 27 amino acids
    - (B) TYPE: AMINO ACID
    - (D) TOPOLOGY: LINEAR
  - (ii) MOLECULE TYPE: PROTEIN
  - (vi) ORIGINAL SOURCE:
    - (A) ORGANISM: Homo Sapiens
    - (F) TISSUE TYPE: Brain
  - (ix) FEATURE:
    - (A) NAME/KEY: sig\_peptide
    - (B) LOCATION: -23..-1
    - (C) IDENTIFICATION METHOD: Von Heijne matrix
    - (D) OTHER INFORMATION: score 4.8

seq VMWLVALLEMCVC/KK

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 344:

Met His Ser Ser Ile Lys Thr Lys Gly Ser Val Met Trp Leu Val Ala

Leu Leu Glu Met Cys Val Cys Lys Lys Ser Arg

- (2) INFORMATION FOR SEQ ID NO: 345:
  - (i) SEQUENCE CHARACTERISTICS:
    - (A) LENGTH: 44 amino acids
    - (B) TYPE: AMINO ACID
    - (D) TOPOLOGY: LINEAR
  - (ii) MOLECULE TYPE: PROTEIN
  - (vi) ORIGINAL SOURCE:
    - (A) ORGANISM: Homo Sapiens
    - (F) TISSUE TYPE: Brain
  - (ix) FEATURE:
    - (A) NAME/KEY: sig\_peptide
    - (B) LOCATION: -18..-1
    - (C) IDENTIFICATION METHOD: Von Heijne matrix
    - (D) OTHER INFORMATION: score 4.8

seq LEAISSLSSFVLG/RM

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 345:

Met Thr Val Leu Pro Leu Glu Ala Ile Ser Ser Leu Ser Ser Phe Val

Leu Gly Arg Net Asn Ser Arg Gly Ala Gly Lys Thr Gln Asn Leu Asp

Ala Ser Ser Leu Leu Leu Cys Cys Leu Ile Leu 20

- (2) INFORMATION FOR SEQ ID NO: 346:
  - (i) SEQUENCE CHARACTERISTICS:
    - (A) LENGTH: 125 amino acids
    - (B) TYPE: AMINO ACID
    - (D) TOPOLOGY: LINEAR
  - (ii) MOLECULE TYPE: PROTEIN
  - (vi) ORIGINAL SOURCE:
    - (A) ORGANISM: Homo Sapiens
    - (F) TISSUE TYPE: Brain
  - (ix) FEATURE:
    - (A) NAME/KEY: sig\_peptide
    - (B) LOCATION: -30..-1
    - (C) IDENTIFICATION METHOD: Von Heijne matrix
    - (D) OTHER INFORMATION: score 4.8

seq ILFCVGAVGACTL/SV

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 346:

Met Gly Thr Ala Ser Arg Ser Asn Ile Ala Arg His Leu Gln Thr Asn

Leu Ile Leu Phe Cys Val Gly Ala Val Gly Ala Cys Thr Leu Ser Val

Thr Gln Pro Trp Tyr Leu Glu Val Asp Tyr Thr His Glu Ala Val Thr

Ile Lys Cys Thr Phe Ser Ala Thr Gly Cys Pro Ser Glu Gln Pro Thr

Cys Leu Trp Phe Arg Tyr Gly Ala His Gln Pro Glu Asn Leu Cys Leu

Asp Gly Cys Lys Ser Glu Ala Xaa Lys Phe Thr Val Arg Glu Ala Leu

Lys Glu Asn Gln Val Ser Leu Thr Val Asn Arg Val Thr Ser Asn Asp

Ser Ala Ile Tyr Ile Cys Gly Ile Ala Phe Pro Ser Val 90

- (2) INFORMATION FOR SEQ ID NO: 347:
  - (i) SEQUENCE CHARACTERISTICS:

WO 99/06552 PCT/IB98/01236

- (A) LENGTH: 46 amino acids
- (B) TYPE: AMINO ACID
- (D) TOPOLOGY: LINEAR
- (ii) MOLECULE TYPE: PROTEIN
- (vi) ORIGINAL SOURCE:
  - (A) ORGANISM: Homo Sapiens
  - (F) TISSUE TYPE: Brain
- (ix) FEATURE:
  - (A) NAME/KEY: sig\_peptide
  - (B) LOCATION: -25..-1
  - (C) IDENTIFICATION METHOD: Von Heijne matrix
  - (D) OTHER INFORMATION: score 4.8

seq ALFYSVVVSTVSG/NE

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 347:

Met Asn Ser Ser Lys Glu Glu Met Arg Glu Leu Ala Ala Leu Phe Tyr
-25 -15 -10

Ser Val Val Ser Thr Val Ser Gly Asn Glu Leu Lys Ser Met Ile
-5 1 5

Glu Gln Leu Ile Lys Thr Thr Lys Asp Asn His Ser Leu Arg 10 15 20

- (2) INFORMATION FOR SEQ ID NO: 348:
  - (i) SEQUENCE CHARACTERISTICS:
    - (A) LENGTH: 81 amino acids
    - (B) TYPE: AMINO ACID
    - (D) TOPOLOGY: LINEAR
  - (ii) MOLECULE TYPE: PROTEIN
  - (vi) ORIGINAL SOURCE:
    - (A) ORGANISM: Homo Sapiens
    - (F) TISSUE TYPE: Brain
  - (ix) FEATURE:
    - (A) NAME/KEY: sig\_peptide
    - (B) LOCATION: -52..-1
    - (C) IDENTIFICATION METHOD: Von Heijne matrix
    - (D) OTHER INFORMATION: score 4.7

seq LLAKALHLLKSSC/AP

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 348:

Met Ser Gln Asp Gly Gly Xaa Gly Glu Leu Lys His Met Val Met Ser
-50 -45 -40

Phe Arg Val Ser Glu Leu Gln Val Leu Leu Gly Phe Ala Gly Arg Asn
-35
-30
-25

Lys Ser Gly Arg Lys His Glu Leu Leu Ala Lys Ala Leu His Leu Leu

-20 -15 -10 -5

Lys Ser Ser Cys Ala Pro Ser Val Gln Met Lys Ile Lys Glu Leu Tyr

1 5 10

Arg Arg Arg Phe Pro Arg Lys Thr Leu Gly Pro Ser Asp Leu Ser Ser

Gly

- (2) INFORMATION FOR SEQ ID NO: 349:
  - (i) SEQUENCE CHARACTERISTICS:
    - (A) LENGTH: 47 amino acids
    - (B) TYPE: AMINO ACID
    - (D) TOPOLOGY: LINEAR
  - (ii) MOLECULE TYPE: PROTEIN
  - (vi) ORIGINAL SOURCE:
    - (A) ORGANISM: Homo Sapiens
    - (F) TISSUE TYPE: Brain
  - (ix) FEATURE:
    - (A) NAME/KEY: sig\_peptide
    - (B) LOCATION: -29..-1
    - (C) IDENTIFICATION METHOD: Von Heijne matrix
    - (D) OTHER INFORMATION: score 4.7 seq LCYLSIFCLGVLF/II
  - (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 349:

Met Pro Cys Ile Ser Leu Leu Gly Leu Leu Tyr Asn Phe Val Gln Val -25 -20 -15

Leu Cys Tyr Leu Ser Ile Phe Cys Leu Gly Val Leu Phe Ile Ile Glu -10 -5 1

Arg Gly Ser Leu Lys Val Ser Lys Leu Ile Cys Arg Pro Pro Gly
5 10 15

- (2) INFORMATION FOR SEQ ID NO: 350:
  - (i) SEQUENCE CHARACTERISTICS:
    - (A) LENGTH: 47 amino acids
    - (B) TYPE: AMINO ACID
    - (D) TOPOLOGY: LINEAR
  - (ii) MOLECULE TYPE: PROTEIN
  - (vi) ORIGINAL SOURCE:
    - (A) ORGANISM: Homo Sapiens
    - (F) TISSUE TYPE: Brain
  - (ix) FEATURE:
    - (A) NAME/KEY: sig\_peptide

- (B) LOCATION: -15..-1
- (C) IDENTIFICATION METHOD: Von Heijne matrix
- (D) OTHER INFORMATION: score 4.7 seq IAVLFCFFLLIIF/QT
- (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 350:

Met Lys Ile Ala Val Leu Phe Cys Phe Phe Leu Leu Ile Ile Phe Gln -15 -5 1

Thr Asp Phe Gly Lys Asn Glu Glu Ile Pro Arg Lys Gln Arg Arg Lys
5 10 15

Ile Tyr His Arg Arg Leu Arg Lys Ser Ser Thr Ser His Lys Gln
20 25 30

- (2) INFORMATION FOR SEQ ID NO: 351:
  - (i) SEQUENCE CHARACTERISTICS:
    - (A) LENGTH: 48 amino acids
    - (B) TYPE: AMINO ACID
    - (D) TOPOLOGY: LINEAR
  - (ii) MOLECULE TYPE: PROTEIN
  - (vi) ORIGINAL SOURCE:
    - (A) ORGANISM: Homo Sapiens
    - (F) TISSUE TYPE: Brain
  - (ix) FEATURE:
    - (A) NAME/KEY: sig peptide
    - (B) LOCATION: -43..-1
    - (C) IDENTIFICATION METHOD: Von Heijne matrix
    - (D) OTHER INFORMATION: score 4.7

seq STWSSASLRGSWQ/QG

- (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 351:
- Met Ala Lys Gln Lys Pro His Val Leu Gly Ser Arg Val Met Pro Ala
  -40 -35 -30

Ser Cys Val Ser Glu Arg Arg Lys Pro Ser Phe Gln Val Ser Thr
-25
-20
-15

Trp Ser Ser Ala Ser Leu Arg Gly Ser Trp Gln Gln Gly Met Pro Gly
-10 -5 1 5

- (2) INFORMATION FOR SEQ ID NO: 352:
  - (i) SEQUENCE CHARACTERISTICS:
    - (A) LENGTH: 17 amino acids
    - (B) TYPE: AMINO ACID
    - (D) TOPOLOGY: LINEAR
  - (ii) MOLECULE TYPE: PROTEIN

(vi) ORIGINAL SOURCE:

(A) ORGANISM: Homo Sapiens

(F) TISSUE TYPE: Brain

(ix) FEATURE:

(A) NAME/KEY: sig\_peptide

(B) LOCATION: -15..-1

- (C) IDENTIFICATION METHOD: Von Heijne matrix
- (D) OTHER INFORMATION: score 4.6

seq FLYLKSVFDVSLG/AR

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 352:

Met Gly Phe Leu Tyr Leu Lys Ser Val Phe Asp Val Ser Leu Gly Ala -15 -5

Arq

- (2) INFORMATION FOR SEQ ID NO: 353:
  - (i) SEQUENCE CHARACTERISTICS:
    - (A) LENGTH: 69 amino acids
    - (B) TYPE: AMINO ACID
    - (D) TOPOLOGY: LINEAR
  - (ii) MOLECULE TYPE: PROTEIN
  - (vi) ORIGINAL SOURCE:
    - (A) ORGANISM: Homo Sapiens
    - (F) TISSUE TYPE: Brain
  - (ix) FEATURE:
    - (A) NAME/KEY: sig\_peptide
    - (B) LOCATION: -61..-1
    - (C) IDENTIFICATION METHOD: Von Heijne matrix
    - (D) OTHER INFORMATION: score 4.6

seg LLLLHGGGHSALS/WA

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 353:

Met Arg Met Gly Pro Gly Arg Lys Arg Asp Phe Ser Pro Val Pro Trp -50 -50

Ser Gln Tyr Phe Glu Ser Met Glu Asp Val Glu Val Glu Ash Glu Thr -45 -40 -35 -30

Gly Lys Asp Thr Phe Arg Val Tyr Lys Ser Gly Ser Glu Gly Pro Val

Leu Leu Leu His Gly Gly Gly His Ser Ala Leu Ser Trp Ala Val

Phe Thr Ala Ala Xaa

WO 99/06552 344

- (2) INFORMATION FOR SEQ ID NO: 354:
  - (i) SEQUENCE CHARACTERISTICS:
    - (A) LENGTH: 23 amino acids
    - (B) TYPE: AMINO ACID
    - (D) TOPOLOGY: LINEAR
  - (ii) MOLECULE TYPE: PROTEIN
  - (vi) ORIGINAL SOURCE:
    - (A) ORGANISM: Homo Sapiens
    - (F) TISSUE TYPE: Brain
  - (ix) FEATURE:
    - (A) NAME/KEY: sig\_peptide
    - (B) LOCATION: -13..-1
    - (C) IDENTIFICATION METHOD: Von Heijne matrix
    - (D) OTHER INFORMATION: score 4.6

seq MIFLLYLLPSSEE/RR

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 354:

Met Ile Phe Leu Leu Tyr Leu Leu Pro Ser Ser Glu Glu Arg Arg Lys

Leu Leu Phe Ser Pro His Arg 5

- (2) INFORMATION FOR SEQ ID NO: 355:
  - (i) SEQUENCE CHARACTERISTICS:
    - (A) LENGTH: 70 amino acids
    - (B) TYPE: AMINO ACID
    - (D) TOPOLOGY: LINEAR
  - (ii) MOLECULE TYPE: PROTEIN
  - (vi) ORIGINAL SOURCE:
    - (A) ORGANISM: Homo Sapiens
    - (F) TISSUE TYPE: Brain
  - (ix) FEATURE:
    - (A) NAME/KEY: sig\_peptide
    - (B) LOCATION: -61..-1
    - (C) IDENTIFICATION METHOD: Von Heijne matrix
    - (D) OTHER INFORMATION: score 4.6

seq LLLLHGGGHSALS/WA

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 355:

Met Arg Met Gly Pro Gly Arg Lys Arg Asp Phe Ser Pro Val Pro Trp -60 **-55** ⋅

Ser Gln Tyr Phe Glu Ser Met Glu Asp Val Glu Val Glu Asn Glu Thr -35

Gly Lys Asp Thr Phe Arg Val Tyr Lys Ser Gly Ser Glu Gly Pro Val -20

Leu Leu Leu His Gly Gly Gly His Ser Ala Leu Ser Trp Ala Val -10 -- 5

Phe Thr Ala Ala Thr Trp

- (2) INFORMATION FOR SEQ ID NO: 356:
  - (i) SEQUENCE CHARACTERISTICS:
    - (A) LENGTH: 30 amino acids
    - (B) TYPE: AMINO ACID
    - (D) TOPOLOGY: LINEAR
  - (ii) MOLECULE TYPE: PROTEIN
  - (vi) ORIGINAL SOURCE:
    - (A) ORGANISM: Homo Sapiens
    - (F) TISSUE TYPE: Brain
  - (ix) FEATURE:
    - (A) NAME/KEY: sig\_peptide
    - (B) LOCATION: -16..-1
    - (C) IDENTIFICATION METHOD: Von Heijne matrix
    - (D) OTHER INFORMATION: score 4.5

seq LLNLISILASIPS/QF

- (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 356:
- Met Leu Ser Leu Leu Asn Leu Ile Ser Ile Leu Ala Ser Ile Pro Ser -10
- Gln Phe Lys Pro Gln Phe Ser Lys Leu Pro Leu Ser Gly Arg
- (2) INFORMATION FOR SEQ ID NO: 357:
  - (i) SEQUENCE CHARACTERISTICS:
    - (A) LENGTH: 28 amino acids
    - (B) TYPE: AMINO ACID
    - (D) TOPOLOGY: LINEAR
  - (ii) MOLECULE TYPE: PROTEIN
  - (vi) ORIGINAL SOURCE:
    - (A) ORGANISM: Homo Sapiens
    - (F) TISSUE TYPE: Brain
  - (ix) FEATURE:
    - (A) NAME/KEY: sig\_peptide
    - (B) LOCATION: -25..-1
    - (C) IDENTIFICATION METHOD: Von Heijne matrix
    - (D) OTHER INFORMATION: score 4.5

seq LMLLWPVHPLLVG/HR

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 357:

Met Gly Thr Thr Ser Asn Met Val Thr Thr Ile His Leu Met Leu Leu -25 -10 -15

Trp Pro Val His Pro Leu Leu Val Gly His Arg Gly
-5

- (2) INFORMATION FOR SEQ ID NO: 358:
  - (i) SEQUENCE CHARACTERISTICS:
    - (A) LENGTH: 147 amino acids
    - (B) TYPE: AMINO ACID
    - (D) TOPOLOGY: LINEAR
  - (ii) MOLECULE TYPE: PROTEIN
  - (vi) ORIGINAL SOURCE:
    - (A) ORGANISM: Homo Sapiens
    - (F) TISSUE TYPE: Brain
  - (ix) FEATURE:
    - (A) NAME/KEY: sig\_peptide
    - (B) LOCATION: -101..-1
    - (C) IDENTIFICATION METHOD: Von Heijne matrix
    - (D) OTHER INFORMATION: score 4.4 seq ISHILAFFAASDG/IV
  - (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 358:

Met Gly Asp Pro Glu Arg Pro Glu Ala Ala Gly Leu Asp Gln Asp Glu

Arg Ser Ser Ser Asp Thr Asn Glu Ser Glu Ile Lys Ser Asn Glu Glu
-85 -75 -70

Pro Leu Leu Arg Lys Ser Ser Arg Arg Phe Val Ile Phe Pro Ile Gln -65 -60 -55

Tyr Pro Asp Ile Trp Lys Met Tyr Lys Gln Ala Gln Ala Ser Phe Trp
-50 -45 -40

Thr Ala Glu Glu Val Asp Leu Ser Lys Asp Leu Pro His Trp Asn Lys
-35
-30
-25

Leu Lys Ala Asp Glu Lys Tyr Phe Ile Ser His Ile Leu Ala Phe Phe -20 -15 -10

Ala Ala Ser Asp Gly Ile Val Asn Glu Asn Leu Val Glu Arg Phe Ser -5 10

Gln Glu Val Gln Val Pro Glu Ala Arg Cys Phe Tyr Gly Phe Gln Ile 15 20 25

Leu Ile Glu Asn Val His Ser Glu Met Tyr Ser Leu Leu Ile Asp Thr 30 35 40

Tyr Ile Arg 45

- (2) INFORMATION FOR SEQ ID NO: 359:
  - (i) SEQUENCE CHARACTERISTICS:
    - (A) LENGTH: 65 amino acids
    - (B) TYPE: AMINO ACID
    - (D) TOPOLOGY: LINEAR
  - (ii) MOLECULE TYPE: PROTEIN
  - (vi) ORIGINAL SOURCE:
    - (A) ORGANISM: Homo Sapiens
    - (F) TISSUE TYPE: Brain
  - (ix) FEATURE:
    - (A) NAME/KEY: sig\_peptide
    - (B) LOCATION: -16..-1
    - ( $\mathbb C$ ) IDENTIFICATION METHOD: Von Heijne matrix
    - (D) OTHER INFORMATION: score 4.4

seq GLFSLLPHPPCVG/RV

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 359:

Met Asp Ala Gly Leu Phe Ser Leu Leu Pro His Pro Pro Cys Val Gly
-15 -10 -5

Arg Val Leu Pro Gln Ser Arg Tyr His Leu His Pro Arg Ser Pro Leu 1 5 10 15

Val Glu Asp Thr Cys Phe Phe Gln Arg Leu Lys Lys Ile Leu Asn Lys 20 25 30

Ile Gly Asn Leu Phe His Ser Thr Lys Ser Leu Cys Val Ser Leu Ala

Pro

- (2) INFORMATION FOR SEQ ID NO: 360:
  - (i) SEQUENCE CHARACTERISTICS:
    - (A) LENGTH: 19 amino acids
    - (B) TYPE: AMINO ACID
    - (D) TOPOLOGY: LINEAR
  - (ii) MOLECULE TYPE: PROTEIN
  - (vi) ORIGINAL SOURCE:
    - (A) ORGANISM: Homo Sapiens
    - (F) TISSUE TYPE: Brain
  - (ix) FEATURE:
    - A) NAME/KEY: sig\_peptide
    - Contion: -14..-1

(C) IDENTIFICATION METHOD: Von Heijne matrix

(D) OTHER INFORMATION: score 4.4 seq LITLTYLIQGESA/RT

(xi) SEQUENCE DESCRIPTION: SEO ID NO: 360:

Met Leu Ile Thr Leu Thr Tyr Leu Ile Gln Gly Glu Ser Ala Arg Thr -10 -5 1

Thr Phe Glu

- (2) INFORMATION FOR SEQ ID NO: 361:
  - (i) SEQUENCE CHARACTERISTICS:
    - (A) LENGTH: 31 amino acids
      - (B) TYPE: AMINO ACID
      - (D) TOPOLOGY: LINEAR
  - (ii) MOLECULE TYPE: PROTEIN
  - (vi) ORIGINAL SOURCE:
    - (A) ORGANISM: Homo Sapiens
    - (F) TISSUE TYPE: Brain
  - (ix) FEATURE:
    - (A) NAME/KEY: sig\_peptide
    - (B) LOCATION: -26..-1
    - (C) IDENTIFICATION METHOD: Von Heijne matrix
    - (D) OTHER INFORMATION: score 4.4

seq RVQCLCAIPFAFS/LT

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 361:

Met Tyr Thr Gly Phe Arg Ile Glu Ala Thr Leu Leu Thr Arg Val Gln
-25
-15

Cys Leu Cys Ala Ile Pro Phe Ala Phe Ser Leu Thr Gly Ile Arg

- (2) INFORMATION FOR SEO ID NO: 362:
  - (i) SEQUENCE CHARACTERISTICS:
    - (A) LENGTH: 56 amino acids
    - (B) TYPE: AMINO ACID
    - (D) TOPOLOGY: LINEAR
  - (ii) MOLECULE TYPE: PROTEIN
  - (vi) ORIGINAL SOURCE:
    - (A) ORGANISM: Homo Sapiens
    - (F) TISSUE TYPE: Brain
  - (ix) FEATURE:
    - (A) NAME/KEY: sig peptide

(B) LOCATION: -47..-1

(C) IDENTIFICATION METHOD: Von Heijne matrix

(D) OTHER INFORMATION: score 4.4 seq ISHILAFFAASDG/IV

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 362:

Met Tyr Lys Gln Ala Gln Ala Ser Phe Trp Thr Ala Glu Glu Val Asp -40

Leu Ser Lys Asp Leu Pro His Trp Asn Lys Leu Lys Ala Asp Glu Lys

Tyr Phe Ile Ser His Ile Leu Ala Phe Phe Ala Ala Ser Asp Gly Ile

Val Asn Glu Asn Leu Val Glu Arg

- (2) INFORMATION FOR SEQ ID NO: 363:
  - (i) SEQUENCE CHARACTERISTICS:
    - (A) LENGTH: 48 amino acids

    - (B) TYPE: AMINO ACID
      (D) TOPOLOGY: LINEAR
  - (ii) MOLECULE TYPE: PROTEIN
  - (vi) ORIGINAL SOURCE:
    - (A) ORGANISM: Homo Sapiens
    - (F) TISSUE TYPE: Brain
  - (ix) FEATURE:
    - (A) NAME/KEY: sig\_peptide
    - (B) LOCATION: -28..-1
    - (C) IDENTIFICATION METHOD: Von Heijne matrix
    - (D) OTHER INFORMATION: score 4.3

seq FLGLAAMASPSRN/SQ

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 363:

Met Leu Leu His Leu Cys Ser Val Lys Asn Leu Tyr Gln Asn Arg Phe

Leu Gly Leu Ala Ala Met Ala Ser Pro Ser Arg Asn Ser Gln Ser Arg -5

Arg Arg Cys Lys Glu Pro Leu Arg Tyr Ser Tyr Asn Pro Asp Gln Gly

- (2) INFORMATION FOR SEQ ID NO: 364:
  - (i) SEQUENCE CHARACTERISTICS:
    - (A) LENGTH: 55 amino acids
    - (B) TYPE: AMINO ACID

(D) TOPOLOGY: LINEAR

- (ii) MOLECULE TYPE: PROTEIN
- (vi) ORIGINAL SOURCE:
  - (A) ORGANISM: Homo Sapiens
  - (F) TISSUE TYPE: Brain
- (ix) FEATURE:
  - (A) NAME/KEY: sig\_peptide
  - (B) LOCATION: -18..-1
  - (C) IDENTIFICATION METHOD: Von Heijne matrix
  - (D) OTHER INFORMATION: score 4.3

seq WTCLKSFPSPTSS/HA

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 364:

Met Pro Cys Pro Thr Trp Thr Cys Leu Lys Ser Phe Pro Ser Pro Thr
-15
-10
-5

Ser Ser His Ala Ser Ser Leu His Leu Pro Pro Ser Cys Thr Arg Leu
1 5 10

Thr Leu Thr Gln Thr Leu Arg Thr Gly Met His Leu Ser Arg Ala Leu 15 20 25 30

Gln Gly Thr Leu Thr Arg Gln

- (2) INFORMATION FOR SEQ ID NO: 365:
  - (i) SEQUENCE CHARACTERISTICS:
    - (A) LENGTH: 73 amino acids
    - (B) TYPE: AMINO ACID
    - (D) TOPOLOGY: LINEAR
  - (ii) MOLECULE TYPE: PROTEIN
  - (vi) ORIGINAL SOURCE:
    - (A) ORGANISM: Homo Sapiens
    - (F) TISSUE TYPE: Brain
  - (ix) FEATURE:
    - (A) NAME/KEY: sig\_peptide
    - (B) LOCATION: -33..-1
    - (C) IDENTIFICATION METHOD: Von Heijne matrix
    - (D) OTHER INFORMATION: score 4.3

seq LLGWGLNLTLGQG/AP

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 365:

Met Glu Asp Leu Phe Ser Pro Ser Ile Xaa Pro Pro Ala Pro Asn Ile
-30 -25 -20

Ser Val Pro Ile Leu Leu Gly Trp Gly Leu Asn Leu Thr Leu Gly Gln
-15 -10 -5

Gly Ala Pro Ala Ser Gly Pro Pro Ser Arg Arg Val Arg Leu Val Phe
1 5 10 15

Leu Gly Val Iie Leu Val Val Aia Val Ala Xaa Asn Thr Thr Val Leu
20 25 30

Cys Arg Leu Cys Gly Gly Gly Pro 35 40

- (2) INFORMATION FOR SEQ ID NO: 366:
  - (i) SEQUENCE CHARACTERISTICS:
    - (A) LENGTH: 55 amino acids
    - (B) TYPE: AMINO ACID
    - (D) TOPOLOGY: LINEAR
  - (ii) MOLECULE TYPE: PROTEIN
  - (vi) ORIGINAL SOURCE:
    - (A) ORGANISM: Homo Sapiens
    - (F) TISSUE TYPE: Brain
  - (ix) FEATURE:
    - (A) NAME/KEY: sig\_peptide
    - (B) LOCATION: -52..-1
    - (C) IDENTIFICATION METHOD: Von Heijne matrix
    - (D) OTHER INFORMATION: score 4.1

seq VMLETCGLLVSLG/HP

- (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 366:
- Met Ala Glu Thr Lys Asp Ala Ala Gln Met Leu Val Thr Phe Lys Asp
  -50 -45 -40
- Val Ala Val Thr Phe Thr Arg Glu Glu Trp Arg Gln Leu Asp Leu Ala -35 -25
- Gln Arg Thr Leu Tyr Arg Glu Val Met Leu Glu Thr Cys Gly Leu Leu  $\sim 20$   $\sim 15$   $\sim 10$   $\sim 5$

Val Ser Leu Gly His Pro Arg

- (2) INFORMATION FOR SEQ ID NO: 367:
  - (i) SEQUENCE CHARACTERISTICS:
    - (A) LENGTH: 45 amino acids
    - (B) TYPE: AMINO ACID
    - (D) TOPOLOGY: LINEAR
  - (ii) MOLECULE TYPE: PROTEIN
  - (vi) ORIGINAL SOURCE:
    - (A) ORGANISM: Homo Sapiens
    - (F) TISSUE TYPE: Brain

(ix) FEATURE:

- (A) NAME/KEY: sig\_peptide
- (B) LOCATION: -13..-1
- (C) IDENTIFICATION METHOD: Von Heijne matrix
- (D) OTHER INFORMATION: score 4.1 seq MLILSQNIAQLEA/QV
- (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 367:

Met Leu Ile Leu Ser Gln Asn Ile Ala Gln Leu Glu Ala Gln Val Glu
-10 -5

Lys Val Thr Lys Glu Lys Ile Ser Ala Ile Asn Gln Leu Glu Glu Asn 5 10 15

Ser Lys Pro Ala Gly Phe Ser Gly Lys Trp Met Ser Gln 20 25 30

- (2) INFORMATION FOR SEQ ID NO: 368:
  - (i) SEQUENCE CHARACTERISTICS:
    - (A) LENGTH: 97 amino acids
    - (B) TYPE: AMINO ACID
    - (D) TOPOLOGY: LINEAR
  - (ii) MOLECULE TYPE: PROTEIN
  - (vi) ORIGINAL SOURCE:
    - (A) ORGANISM: Homo Sapiens
    - (F) TISSUE TYPE: Brain
  - (ix) FEATURE:
    - (A) NAME/KEY: sig peptide
    - (B) LOCATION: -21..-1
    - (C) IDENTIFICATION METHOD: Von Heijne matrix
    - (D) OTHER INFORMATION: score 4.1 seq GLWAHSWTCSCSA/AX
  - (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 368:

Met Leu Leu Gly Ala Ser Ala Gln Gly Leu Trp Ala His Ser Trp Thr
-20 -15 -10

Cys Ser Cys Ser Ala Ala Xaa Arg Ser Val His Pro Gly Gly Asp Trp -5 10

Met Gln Gln Phe Gln Ala Gly Phe Leu Pro Pro Gln Val Pro Ala His
15 20 25

Leu Ser Leu Thr Trp Asp Val Ser Leu Leu Pro Pro Cys Leu Val Pro 30 35 40

Lys Ala Leu Glu Phe Val Val His Phe Leu Lys Asn Asp Ile Phe Tyr 45 50 55

Leu Thr Gln Tyr Ile Lys Asn Val Ile Ser Glu Cys Thr Phe Ser Phe 60 70 75

Phe

- (2) INFORMATION FOR SEQ ID NO: 369:
  - (i) SEQUENCE CHARACTERISTICS:
    - (A) LENGTH: 68 amino acids
    - (B) TYPE: AMINO ACID
    - (D) TOPOLOGY: LINEAR
  - (ii) MOLECULE TYPE: PROTEIN
  - (vi) ORIGINAL SOURCE:
    - (A) ORGANISM: Homo Sapiens
    - (F) TISSUE TYPE: Brain
  - (ix) FEATURE:
    - (A) NAME/KEY: sig\_peptide
    - (B) LOCATION: -15..-1
    - (C) IDENTIFICATION METHOD: Von Heijne matrix
    - (D) OTHER INFORMATION: score 4.1

seq APLELSCWGGGWG/LP

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 369:

Met Ala Ala Pro Leu Glu Leu Ser Cys Trp Gly Gly Gly Trp Gly Leu

Pro Ser Val His Ser Glu Ser Leu Val Val Met Ala Tyr Ala Lys Phe

Ser Gly Ala Pro Leu Lys Val Asn Val Ile Asp Asn Thr Trp Arg Gly

Ser Arg Gly Asp Val Pro Ile Leu Thr Thr Glu Asp Asp Met Val Ser 35 40

Gln Pro Ala Arg 50

- (2) INFORMATION FOR SEQ ID NO: 370:
  - (i) SEQUENCE CHARACTERISTICS:
    - (A) LENGTH: 69 amino acids
    - (B) TYPE: AMINO ACID
    - (D) TOPOLOGY: LINEAR
  - (ii) MOLECULE TYPE: PROTEIN
  - (vi) ORIGINAL SOURCE:
    - (A) ORGANISM: Homo Sapiens
    - (F) TISSUE TYPE: Brain
  - (ix) FEATURE:
    - (A) NAME/KEY: sig\_peptide
    - (C) LOCATION: -20..-1

(C) IDENTIFICATION METHOD: Von Heijne matrix

(D) OTHER INFORMATION: score 4.1 seq LGFLNCYIAVARS/GG

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 370:

Met Ser Xaa Val Gly Ile Asp Leu Gly Phe Leu Asn Cys Tyr Ile Ala
-20 -15 -10 -5

Val Ala Arg Ser Gly Gly Ile Glu Thr Ile Ala Asn Glu Tyr Ser Asp 1 5 10

Arg Cys Thr Pro Ala Cys Ile Ser Leu Gly Ser Arg Thr Arg Ala Ile
15 20 25

Gly Asn Ala Ala Lys Ser Gln Ile Val Thr Asn Val Arg Asn Thr Ile 30 40

His Gly Phe Lys Lys 45

- (2) INFORMATION FOR SEQ ID NO: 371:
  - (i) SEQUENCE CHARACTERISTICS:
    - (A) LENGTH: 43 amino acids
    - (B) TYPE: AMINO ACID
    - (D) TOPOLOGY: LINEAR
  - (ii) MOLECULE TYPE: PROTEIN
  - (vi) ORIGINAL SOURCE:
    - (A) ORGANISM: Homo Sapiens
    - (F) TISSUE TYPE: Brain
  - (ix) FEATURE:
    - (A) NAME/KEY: sig\_peptide
    - (B) LOCATION: -19..-1
    - (C) IDENTIFICATION METHOD: Von Heijne matrix
    - (D) OTHER INFORMATION: score 4.1 seq FVVFSTMFTASSP/GE
  - (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 371:

Met Glu Tyr Ser Lys Xaa Phe Val Val Phe Ser Thr Met Phe Thr Ala
-15 -10 -5

Ser Ser Pro Gly Glu Asp Phe Pro Pro Phe Phe Ser Gln Met Xaa Arg

1 5 10

Leu Ser Arg Asn Tyr Phe Pro Cys Pro Pro Xaa 15 20

- (2) INFORMATION FOR SEQ ID NO: 372:
  - (i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 72 amino acids

- (B) TYPE: AMINO ACID
- (D) TOPOLOGY: LINEAR
- (ii) MOLECULE TYPE: PROTEIN
- (vi) ORIGINAL SOURCE:
  - (A) ORGANISM: Homo Sapiens
  - (F) TISSUE TYPE: Brain
- (ix) FEATURE:
  - (A) NAME/KEY: sig\_peptide
  - (B) LOCATION: -40..-1
  - (C) IDENTIFICATION METHOD: Von Heijne matrix
  - (D) OTHER INFORMATION: score 4.1 seq LPFRLPWASTATA/RC
- (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 372:

Met Pro Met Ala Ser Ser Pro Pro Pro Ser Pro His Pro Gln Glu Pro -40 -35 -30 -30

Ala Pro Leu Leu Pro Ser Leu Pro Arg Leu Ser Leu Pro Phe Arg Leu -20 -15 -10

Pro Trp Ala Ser Thr Ala Thr Ala Arg Cys Pro Pro Ser Pro Leu Gly
-5 1 5

Ser Leu Xaa Leu Met Leu Cys Ile Pro Thr Gly Phe Thr Pro Thr Gln 10 15 20

Pro Arg Ala Pro Arg Pro Pro Gly
25 30

- (2) INFORMATION FOR SEQ ID NO: 373:
  - (i) SEQUENCE CHARACTERISTICS:
    - (A) LENGTH: 55 amino acids
    - (B) TYPE: AMINO ACID
    - (D) TOPOLOGY: LINEAR
  - (ii) MOLECULE TYPE: PROTEIN
  - (vi) ORIGINAL SOURCE:
    - (A) ORGANISM: Homo Sapiens
    - (F) TISSUE TYPE: Brain
  - (ix) FEATURE:
    - (A) NAME/KEY: sig\_peptide
    - (B) LOCATION: -38..-1
    - (C) IDENTIFICATION METHOD: Von Heijne matrix
    - (D) OTHER INFORMATION: score 4

seq WALGLKFLSSSSQ/NF

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 373:

Met Gln His Val Xaa Gly His Xaa Pro Asp Pro Ile Ala Ile Met Tyr

-35 -30 -25

Val Cys Pro Pro Cys Gly His Thr Thr Trp Ala Leu Gly Leu Lys Phe
-20 -15 -10

Leu Ser Ser Ser Ser Gln Asn Phe Cys Ala Pro Val Leu Phe Leu Ile
-5 1 5 10

Leu His Thr Gly Gly Gln Arg 15

- (2) INFORMATION FOR SEQ ID NO: 374:
  - (i) SEQUENCE CHARACTERISTICS:
    - (A) LENGTH: 53 amino acids
      - (B) TYPE: AMINO ACID
      - (D) TOPOLOGY: LINEAR
    - (ii) MOLECULE TYPE: PROTEIN
    - (vi) ORIGINAL SOURCE:
      - (A) ORGANISM: Homo Sapiens
      - (F) TISSUE TYPE: Brain
    - (ix) FEATURE:
      - (A) NAME/KEY: sig\_peptide
        - (B) LOCATION: -30..-1
        - (C) IDENTIFICATION METHOD: Von Heijne matrix
        - (D) OTHER INFORMATION: score 4 seq AGFLKCLLLSSLQ/SY
    - (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 374:

Met Gly Trp Glu Met Thr Cys Ile Lys Ser Phe Phe Trp Ala Arg Ser
-30 -25 -20 -15

His Ala Gly Phe Leu Lys Cys Leu Leu Ser Ser Leu Gln Ser Tyr
-10 -5

Lys Glu Ala Ala Val Ile Phe Pro Leu Thr Asp Leu Leu Lys 5 10 15

Asp Tyr Gly Glu Trp 20

- (2) INFORMATION FOR SEQ ID NO: 375:
  - (i) SEQUENCE CHARACTERISTICS:
    - (A) LENGTH: 38 amino acids
    - (B) TYPE: AMINO ACID
    - (D) TOPOLOGY: LINEAR
  - (ii) MOLECULE TYPE: PROTEIN
  - (vi) ORIGINAL SOURCE:
    - (A) ORGANISM: Homo Sapiens

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(F) TISSUE TYPE: Brain

- (ix) FEATURE:
  - (A) NAME/KEY: sig\_peptide
  - (B) LOCATION: -36..-1
  - (C) IDENTIFICATION METHOD: Von Heijne matrix
  - (D) OTHER INFORMATION: score 4

seq VQLSFAATTPVLA/DK

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 375:

Met Val Phe Gly Gly Val Cys Pro Ser Val Thr Ser Ile Ile Ala Glu

Ser Leu Gln Gly Trp Asn Leu Val Gln Leu Ser Phe Ala Ala Thr Thr -10

Pro Val Leu Ala Asp Lys

- (2) INFORMATION FOR SEQ ID NO: 376:
  - (i) SEQUENCE CHARACTERISTICS:
    - (A) LENGTH: 24 amino acids
    - (B) TYPE: AMINO ACID
    - (D) TOPOLOGY: LINEAR
  - (ii) MOLECULE TYPE: PROTEIN
  - (vi) ORIGINAL SOURCE:
    - (A) ORGANISM: Homo Sapiens
    - (F) TISSUE TYPE: Brain
  - (ix) FEATURE:
    - (A) NAME/KEY: sig\_peptide
    - (B) LOCATION: -16..-1
    - (C) IDENTIFICATION METHOD: Von Heijne matrix
    - (D) OTHER INFORMATION: score 4

seq ITWSLLFLYQCSL/HF

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 376:

Met His Phe Ile Thr Trp Ser Leu Leu Phe Leu Tyr Gln Cys Ser Leu -15 -10

His Phe Ile Ile Lys Ala Gly

- (2) INFORMATION FOR SEQ ID NO: 377:
  - (i) SEQUENCE CHARACTERISTICS:
    - (A) LENGTH: 41 amino acids
    - (B) TYPE: AMINO ACID
    - (D) TOPOLOGY: LINEAR

- (ii) MOLECULE TYPE: PROTEIN
- (vi) ORIGINAL SOURCE:
  - (A) ORGANISM: Homo Sapiens
  - (F) TISSUE TYPE: Brain
- (ix) FEATURE:
  - (A) NAME/KEY: sig\_peptide
  - (B) LOCATION: -36..-1
  - (C) IDENTIFICATION METHOD: Von Heijne matrix
  - (D) OTHER INFORMATION: score 3.9

seq CWPSVASPSSSWS/SP

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 377:

Met Ser Gly Ala Ser Pro Ile Glu Arg Thr Pro Met Glu Glu Ala Pro
-35 -25

Ser Ser Cys Pro Thr Ser Ser Cys Trp Pro Ser Val Ala Ser Pro Ser -20 -15 -10 -5

Ser Ser Trp Ser Ser Pro Trp Ala Ser

- (2) INFORMATION FOR SEQ ID NO: 378:
  - (i) SEQUENCE CHARACTERISTICS:
    - (A) LENGTH: 50 amino acids
    - (B) TYPE: AMINO ACID
    - (D) TOPOLOGY: LINEAR
  - (ii) MOLECULE TYPE: PROTEIN
  - (vi) ORIGINAL SOURCE:
    - (A) ORGANISM: Homo Sapiens
    - (F) TISSUE TYPE: Brain
  - (ix) FEATURE:
    - (A) NAME/KEY: sig\_peptide
    - (B) LOCATION: -37..-1
    - (C) IDENTIFICATION METHOD: Von Heijne matrix
    - (D) OTHER INFORMATION: score 3.9

seq PGPSLRLFSGSQA/SV

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 378:

Net Glu Trp Ala Gly Lys Gln Arg Asp Phe Gln Val Arg Ala Ala Pro
-35 -30 -25

Gly Trp Asp His Leu Ala Ser Phe Pro Gly Pro Ser Leu Arg Leu Phe
-20 -15

Ser Gly Ser Gln Ala Ser Val Cys Ser Leu Cys Ser Gly Phe Gly Ala -5 5 10

Gin Glu

(2) INFORMATION FOR SEQ ID NO: 379:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 67 amino acids
- (B) TYPE: AMINO ACID
- (D) TOPOLOGY: LINEAR
- (ii) MOLECULE TYPE: PROTEIN
- (vi) ORIGINAL SOURCE:
  - (A) ORGANISM: Homo Sapiens
  - (F) TISSUE TYPE: Brain
- (ix) FEATURE:
  - (A) NAME/KEY: sig\_peptide
  - (B) LOCATION: -60..-1
  - (C) IDENTIFICATION METHOD: Von Heijne matrix
  - (D) OTHER INFORMATION: score 3.9

seq AKVVSLSLQTSSA/HH

(x1) SEQUENCE DESCRIPTION: SEQ ID NO: 379:

Met Ile Ala Phe Phe Asp Glu Asp Asn Pro Arg Lys Arg Arg Ser Tyr
-60 -55 -50 -50

Ser Phe Thr Gln Ser Ala Gly Ile Leu Cys Gln Glu Thr Thr Tyr Ser
-40 -35 -30

Thr Pro His Thr Lys Leu Glu Lys Ala Lys Ser Pro Thr Ala Asp Ala
-25 -20 -15

Lys Val Val Ser Leu Ser Leu Gln Thr Ser Ser Ala His His Arg Gly

Gly Xaa Gly

- (2) INFORMATION FOR SEQ ID NO: 380:
  - (i) SEQUENCE CHARACTERISTICS:
    - (A) LENGTH: 87 amino acids
    - (B) TYPE: AMINO ACID
    - (D) TOPOLOGY: LINEAR
  - (ii) MOLECULE TYPE: PROTEIN
  - (vi) ORIGINAL SOURCE:
    - (A) ORGANISM: Homo Sapiens
    - (F) TISSUE TYPE: Brain
  - (ix) FEATURE:
    - (A) NAME/KEY: sig\_peptide
    - (B) LOCATION: -48..-1
    - (C) IDENTIFICATION METHOD: Von Heijne matrix
    - (D) OTHER INFORMATION: score 3.9

seq ALFCTLPCPVERG/QQ

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 380:

Met Gly Lys Ser Ile Xaa Ser Leu Cys Ser Val Xaa Leu Lys Ala Arg
-45 -40 -35

Leu Lys Gly Xaa Leu Glu Ala Val His Leu Cys Leu Arg Ala Gln Lys
-30 -25 -20

Arg Arg Thr Ala Leu Phe Cys Thr Leu Pro Cys Pro Val Glu Arg Gly
-15 -5

Gln Gln Val Pro Gly Xaa Xaa Xaa Arg Leu Arg Leu Ala Ser Pro Ser 1 5 10 15

Val Ala Lys Val Phe Gln Cys Phe Leu Ser Lys Leu Cys Val Trp Asn 20 25 30

Ile Lys Asp Gly Leu Ser Arg 35

- (2) INFORMATION FOR SEQ ID NO: 381:
  - (i) SEQUENCE CHARACTERISTICS:
    - (A) LENGTH: 53 amino acids
    - (B) TYPE: AMINO ACID
    - (D) TOPOLOGY: LINEAR
  - (ii) MOLECULE TYPE: PROTEIN
  - (vi) ORIGINAL SOURCE:
    - (A) ORGANISM: Homo Sapiens
    - (F) TISSUE TYPE: Brain
  - (ix) FEATURE:
    - (A) NAME/KEY: sig\_peptide
    - (B) LOCATION: -15..-1
    - (C) IDENTIFICATION METHOD: Von Heijne matrix
    - (D) OTHER INFORMATION: score 3.9 seq LHMTLFRVPFTFS/XF
  - (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 381:

Met Cys Leu His Met Thr Leu Phe Arg Val Pro Phe Thr Phe Ser Xaa -15 -10 -5 1

Phe Trp Lys Gly Ala Gly Arg Gln Glu Glu Cys Ser Phe Lys Pro Ser 5 10

Leu Tyr Tyr Lys Leu Ile Met Val Leu Lys Ile Ala Leu Leu Leu 20 25 30

Ser Pro Pro Pro Lys

(?) INFORMATION FOR SEQ ID NO: 382:

- (i) SEQUENCE CHARACTERISTICS:
  - (A) LENGTH: 23 amino acids
  - (B) TYPE: AMINO ACID
  - (D) TOPOLOGY: LINEAR
- (ii) MOLECULE TYPE: PROTEIN
- (vi) ORIGINAL SOURCE:
  - (A) ORGANISM: Homo Sapiens
  - (F) TISSUE TYPE: Brain
- (ix) FEATURE:
  - (A) NAME/KEY: sig\_peptide
  - (B) LOCATION: -14..-1
  - (C) IDENTIFICATION METHOD: Von Heijne matrix
  - (D) OTHER INFORMATION: score 3.9 seq LNILKTLTSAALP/SP
- (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 382:

Met Leu Asn Ile Leu Lys Thr Leu Thr Ser Ala Ala Leu Pro Ser Pro

Ser Pro Arg Pro Asn Lys Arg

- (2) INFORMATION FOR SEQ ID NO: 383:
  - (i) SEQUENCE CHARACTERISTICS:
    - (A) LENGTH: 51 amino acids
    - (B) TYPE: AMINO ACID
    - (D) TOPOLOGY: LINEAR
  - (ii) MOLECULE TYPE: PROTEIN
  - (vi) ORIGINAL SOURCE:
    - (A) ORGANISM: Homo Sapiens
    - (F) TISSUE TYPE: Brain
  - (ix) FEATURE:
    - (A) NAME/KEY: sig\_peptide
    - (B) LOCATION: -40..-1
    - (C) IDENTIFICATION METHOD: Von Heijne matrix
    - (D) OTHER INFORMATION: score 3.9

sed SPLLCLYHPPVYT/ST

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 383:

Most Arg Ala Arg Val Trp Pro Arg Ser His Gly Ile Pro Val Pro Ser -45 -35 -30 -25

Ph+ Leu Ser Lys Ser Ser Leu Ser His Thr Pro Ser Pro Leu Leu Cys
-20 -15 -10

Los Tyr His Pro Pro Val Tyr Thr Ser Thr Thr Thr Pro Ser Ile Pro

-5· 1

Pro Arg Leu 10

- (2) INFORMATION FOR SEQ ID NO: 384:
  - (i) SEQUENCE CHARACTERISTICS:
    - (A) LENGTH: 51 amino acids
    - (B) TYPE: AMINO ACID
    - (D) TOPOLOGY: LINEAR
  - (ii) MOLECULE TYPE: PROTEIN
  - (vi) ORIGINAL SOURCE:
    - (A) ORGANISM: Homo Sapiens
    - (F) TISSUE TYPE: Brain
  - (ix) FEATURE:
    - (A) NAME/KEY: sig\_peptide
    - (B) LOCATION: -36..-1
    - (C) IDENTIFICATION METHOD: Von Heijne matrix
    - (D) OTHER INFORMATION: score 3.9

seq SLCLSLLIPGPKP/LV

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 384:

Met Trp Asn Ala Val Ala Ile Ile Cys Asn Gly Ser Trp Cys Gln Thr
-35 -30 -25

Xaa Ser Thr Ser Gly Leu Glu Ser Leu Cys Leu Ser Leu Leu Ile Pro
-20 -15 -10 -5

Gly Pro Lys Pro Leu Val Ser Val Gly Ile Asn Gln Leu Leu Thr
1 5 10

Ser Ser Arg

- (2) INFORMATION FOR SEQ ID NO: 385:
  - (i) SEQUENCE CHARACTERISTICS:
    - (A) LENGTH: 23 amino acids
    - (B) TYPE: AMINO ACID
    - (D) TOPOLOGY: LINEAR
  - (ii) MOLECULE TYPE: PROTEIN
  - (vi) ORIGINAL SOURCE:
    - (A) ORGANISM: Homo Sapiens
    - (F) TISSUE TYPE: Brain
  - (ix) FEATURE:
    - (A) NAME/KEY: sig\_peptide
    - (B) LOCATION: -14..-1
    - (C) IDENTIFICATION METHOD: Von Heijne matrix

(D) OTHER INFORMATION: score 3.9

seq LRLGLFKISWARC/LS

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 385:

Met Leu Arg Leu Gly Leu Phe Lys Ile Ser Trp Ala Arg Cys Leu Ser

Tyr Ser Lys Thr Gln Xaa Glu 5

- (2) INFORMATION FOR SEQ ID NO: 386:
  - (i) SEQUENCE CHARACTERISTICS:
    - (A) LENGTH: 61 amino acids
    - (B) TYPE: AMINO ACID
    - (D) TOPOLOGY: LINEAR
  - (ii) MOLECULE TYPE: PROTEIN
  - (vi) ORIGINAL SOURCE:
    - (A) ORGANISM: Homo Sapiens
    - (F) TISSUE TYPE: Brain
  - (ix) FEATURE:
    - (A) NAME/KEY: sig\_peptide
    - (B) LOCATION: -36..-1
    - (C) IDENTIFICATION METHOD: Von Heijne matrix
    - (D) OTHER INFORMATION: score 3.9

seq VVEILPYLPCLTA/RD

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 386:

Met Pro Phe Ala Glu Asp Lys Thr Tyr Lys Tyr Ile Cys Arg Asn Phe

Ser Asn Phe Cys Asn Val Asp Val Val Glu Ile Leu Pro Tyr Leu Pro -20 -15 -10 -5

Cys Leu Thr Ala Arg Asp Gln Asp Arg Leu Arg Ala Thr Cys Thr Leu  $1 \hspace{1.5cm} 5 \hspace{1.5cm} 10$ 

Ser Gly Asn Arg Asp Thr Leu Trp His Leu Phe Asn Thr
15 20 25

- (2) INFORMATION FOR SEQ ID NO: 387:
  - (1) SEQUENCE CHARACTERISTICS:
    - (A) LENGTH: 40 amino acids
    - (B) TYPE: AMINO ACID
    - (D) TOPOLOGY: LINEAR
  - (ii) MOLECULE TYPE: PROTEIN
  - (vi) ORIGINAL SOURCE:

- (A) ORGANISM: Homo Sapiens
  - (F) TISSUE TYPE: Brain
- (ix) FEATURE:
  - (A) NAME/KEY: sig\_peptide
  - (B) LOCATION: -36..-1
  - (C) IDENTIFICATION METHOD: Von Heijne matrix
  - (D) OTHER INFORMATION: score 3.8

seq GTDSLSFLPPCPC/CP

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 387:

Met Pro Gly Ser Ser Gly Leu Arg Phe Ile Cys Lys Ser Arg Asn His -35 -25

Pro Gln Phe Gly Ser Phe Ser Gly Thr Asp Ser Leu Ser Phe Leu Pro
-20 -15 -10 -5

Pro Cys Pro Cys Cys Pro Ala Ala

- (2) INFORMATION FOR SEQ ID NO: 388:
  - (i) SEQUENCE CHARACTERISTICS:
    - (A) LENGTH: 66 amino acids
    - (B) TYPE: AMINO ACID
    - (D) TOPOLOGY: LINEAR
  - (ii) MOLECULE TYPE: PROTEIN
  - (vi) ORIGINAL SOURCE:
    - (A) ORGANISM: Homo Sapiens
    - (F) TISSUE TYPE: Brain
  - (ix) FEATURE:
    - (A) NAME/KEY: sig\_peptide
    - (B) LOCATION: -57..-1
    - (C) IDENTIFICATION METHOD: Von Heijne matrix
    - (D) OTHER INFORMATION: score 3.8

seq QLXLVMEFCGAGS/VT

- (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 388:
- Met Asp Val Thr Gly Asp Glu Glu Glu Glu Ile Lys Gln Glu Ile Asn
  -55 -50 -45

Met Leu Lys Lys Tyr Ser His His Arg Asn Ile Ala Thr Tyr Tyr Gly
-40 -35 -30

Ala Phe Ile Lys Lys Asn Pro Pro Gly Met Asp Asp Gln Leu Xaa Leu -25 -15 -10

Val Met Glu Phe Cys Gly Ala Gly Ser Val Thr Asp Leu Ile Lys Asn -5 1 5

Thr Gly

(2) INFORMATION FOR SEQ ID NO: 389: (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 26 amino acids (B) TYPE: AMINO ACID (D) TOPOLOGY: LINEAR (ii) MOLECULE TYPE: PROTEIN (vi) ORIGINAL SOURCE: (A) ORGANISM: Homo Sapiens (F) TISSUE TYPE: Brain (ix) FEATURE: (A) NAME/KEY: sig\_peptide (B) LOCATION: -24..-1 (C) IDENTIFICATION METHOD: Von Heijne matrix (D) OTHER INFORMATION: score 3.8 seq KLFLVFLLNICKG/IV (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 389: Met Ile Phe Gly Leu Tyr Phe Val Leu Ala Val Lys Leu Phe Leu Val -20 -15 Phe Leu Leu Asn Ile Cys Lys Gly Ile Val -5 (2) INFORMATION FOR SEQ ID NO: 390: (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 46 amino acids (B) TYPE: AMINO ACID (D) TOPOLOGY: LINEAR (ii) MOLECULE TYPE: PROTEIN (vi) ORIGINAL SOURCE: (A) ORGANISM: Homo Sapiens (F) TISSUE TYPE: Brain (ix) FEATURE: (A) NAME/KEY: sig\_peptide (B) LOCATION: -34...-1(C) IDENTIFICATION METHOD: Von Heijne matrix (D) OTHER INFORMATION: score 3.6 seq IKCSSWISSLASG/IP (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 390: Met Arg Lys Lys Arg Val Glu Glu Leu Ile Val Phe Pro Gly Glu Val -25

Thr Ser Phe Ser Ser Ile Lys Cys Ser Ser Trp Ile Ser Ser Leu Ala

-:0

-15

Ser Gly Ile Pro His Ser Leu Gly Phe Ser Leu Pro Pro Gly
1 5 10

- (2) INFORMATION FOR SEQ ID NO: 391:
  - (i) SEQUENCE CHARACTERISTICS:
    - (A) LENGTH: 57 amino acids
    - (B) TYPE: AMINO ACID
    - (D) TOPOLOGY: LINEAR
  - (ii) MOLECULE TYPE: PROTEIN
  - (vi) ORIGINAL SOURCE:
    - (A) ORGANISM: Homo Sapiens
    - (F) TISSUE TYPE: Brain
  - (ix) FEATURE:
    - (A) NAME/KEY: sig\_peptide
    - (B) LOCATION: -28..-1
    - (C) IDENTIFICATION METHOD: Von Heijne matrix
    - (D) OTHER INFORMATION: score 3.6

seq ACLFSXFLAVSRH/PN

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 391:

Met Pro Ser Ser Leu Ala Glu Leu Cys Leu Met Gln Gln Asp Ala
-25
-20
-15

Cys Leu Phe Ser Xaa Phe Leu Ala Val Ser Arg His Pro Asn Tyr Xaa
-10 -5

Cys Ser Ile Ser Thr Lys Gly Glu Val Arg Glu Lys Leu Val Pro Trp
5 10 15 20

Ile Thr His Gln Met Ala Arg Met Leu 25

- (2) INFORMATION FOR SEQ ID NO: 392:
  - (i) SEQUENCE CHARACTERISTICS:
    - (A) LENGTH: 46 amino acids
    - (B) TYPE: AMINO ACID
    - (D) TOPOLOGY: LINEAR
  - (ii) MOLECULE TYPE: PROTEIN
  - (vi) ORIGINAL SOURCE:
    - (A) ORGANISM: Homo Sapiens
    - (F) TISSUE TYPE: Brain
  - (ix) FEATURE:
    - (A) NAME/KEY: sig\_peptide
    - (B) LOCATION: -40..-1
    - (C) IDENTIFICATION METHOD: Von Heijne matrix
    - (D) OTHER INFORMATION: score 3.6

seq LQMRMQLPCLVLG/EE

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 392:

Met Asp Leu Trp Ser Cys Leu Phe Pro Val Met Leu Met Glu Pro Ser

Lys Gly Leu Glu Asp Ser Glu Trp Lys Met Ala Leu Gln Met Arg Met
-20 -15 -10

Gln Leu Pro Cys Leu Val Leu Gly Glu Glu Gln Thr Leu Gly
-5 1 5

- (2) INFORMATION FOR SEQ ID NO: 393:
  - (i) SEQUENCE CHARACTERISTICS:
    - (A) LENGTH: 37 amino acids
    - (B) TYPE: AMINO ACID
    - (D) TOPOLOGY: LINEAR
  - (ii) MOLECULE TYPE: PROTEIN
  - (vi) ORIGINAL SOURCE:
    - (A) ORGANISM: Homo Sapiens
    - (F) TISSUE TYPE: Brain
  - (ix) FEATURE:
    - (A) NAME/KEY: sig\_peptide
    - (B) LOCATION: -27..-1
    - (C) IDENTIFICATION METHOD: Von Heijne matrix
    - (D) OTHER INFORMATION: score 3.6 seq AVPLPTTSTLTSA/ST
  - (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 393:

Met Ser Gly Lys Gly Lys Cys Arg Pro Ile Ala Leu Arg Arg Ala Val

Pro Leu Pro Thr Thr Ser Thr Leu Thr Ser Ala Ser Thr Gly Phe Leu
-10 -5 1

Trp Ile Leu Lys Glu

- (2) INFORMATION FOR SEQ ID NO: 394:
  - (i) SEQUENCE CHARACTERISTICS:
    - (A) LENGTH: 26 amino acids
    - (B) TYPE: AMINO ACID
    - (D) TOPOLOGY: LINEAR
  - (ii) MOLECULE TYPE: PROTEIN
  - (vi) ORIGINAL SOURCE:
    - (A) ORGANISM: Homo Sapiens

(F) TISSUE TYPE: Brain

- (ix) FEATURE:
  - (A) NAME/KEY: sig\_peptide
  - (B) LOCATION: -18..-1
  - (C) IDENTIFICATION METHOD: Von Heijne matrix
  - (D) OTHER INFORMATION: score 3.6

seq IQKSSGLFCPSQA/QS

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 394:

Met Thr Pro Lys Ala Ile Gln Lys Ser Ser Gly Leu Phe Cys Pro Ser
-15 -10 -5

Gin Ala Gin Ser Ala Arg Pro Ala Glu Lys
1 5

- (2) INFORMATION FOR SEQ ID NO: 395:
  - (i) SEQUENCE CHARACTERISTICS:
    - (A) LENGTH: 103 amino acids
    - (B) TYPE: AMINO ACID
    - (D) TOPOLOGY: LINEAR
  - (ii) MOLECULE TYPE: PROTEIN
  - (vi) ORIGINAL SOURCE:
    - (A) ORGANISM: Homo Sapiens
    - (F) TISSUE TYPE: Brain
  - (ix) FEATURE:
    - (A) NAME/KEY: sig\_peptide
    - (B) LOCATION: -72..-1
    - (C) IDENTIFICATION METHOD: Von Heijne matrix
    - (D) OTHER INFORMATION: score 3.6

seq CTSLLQLYDASNS/EW

- (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 395:
- Met Pro Asp Gln Phe Asp Gln Ala Val Val Leu Asn Gln Leu Arg Tyr
  -70 -65 -60
- Ser Gly Met Leu Glu Thr Val Arg Ile Arg Lys Ala Gly Tyr Ala Val -55 -45
- Arg Arg Pro Phe Gln Asp Phe Tyr Lys Arg Tyr Lys Val Leu Met Arg -40 -35 -30 -25
- Asn Leu Ala Leu Pro Glu Asp Val Arg Gly Lys Cys Thr Ser Leu Leu
  -20 -15 -10
- Gln Leu Tyr Asp Ala Ser Asn Ser Glu Trp Gln Leu Gly Lys Thr Lys
  -5 1 5
- Val Phe Leu Arg Glu Ser Leu Glu Gln Lys Leu Glu Lys Arg Arg Glu
  10 20

Glu Glu Val Ser His Ala Gly 25 30

- (2) INFORMATION FOR SEQ ID NO: 396:
  - (i) SEQUENCE CHARACTERISTICS:
    - (A) LENGTH: 19 amino acids
    - (B) TYPE: AMINO ACID
    - (D) TOPOLOGY: LINEAR
  - (ii) MOLECULE TYPE: PROTEIN
  - (vi) ORIGINAL SOURCE:
    - (A) ORGANISM: Homo Sapiens
    - (F) TISSUE TYPE: Brain
  - (ix) FEATURE:
    - (A) NAME/KEY: sig\_peptide
    - (B) LOCATION: -15..-1
    - (C) IDENTIFICATION METHOD: Von Heijne matrix
    - (D) OTHER INFORMATION: score 3.6

seq LVSFFLELNVLOO/WP

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 396:

Met Cys Leu Val Ser Phe Phe Leu Glu Leu Asn Val Leu Gln Gln Trp
-15 -5

Pro Ala Gly

- (2) INFORMATION FOR SEQ ID NO: 397:
  - (i) SEQUENCE CHARACTERISTICS:
    - (A) LENGTH: 44 amino acids
    - (B) TYPE: AMINO ACID
    - (D) TOPOLOGY: LINEAR
  - (ii) MOLECULE TYPE: PROTEIN
  - (vi) ORIGINAL SOURCE:
    - (A) ORGANISM: Homo Sapiens
    - (F) TISSUE TYPE: Brain
  - (ix) FEATURE:
    - (A) NAME/KEY: sig\_peptide
    - (B) LOCATION: -13..-1
    - (C) IDENTIFICATION METHOD: Von Heijne matrix
    - (D) OTHER INFORMATION: score 3.6

seq MRSLACLTPCGHA/GS

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 397:

Met Arg Ser Leu Ala Cys Leu Thr Pro Cys Gly His Ala Gly Ser Arg

Leu Gln Ser Ser Leu Ser Lys Tyr Leu Val Leu Pro Asn Leu Glu Cys
5 10 15

Leu Phe Phe Leu Phe Leu Ile Ser Asn Arg Arg Trp 20 25 30

- (2) INFORMATION FOR SEQ ID NO: 398:
  - (i) SEQUENCE CHARACTERISTICS:
    - (A) LENGTH: 82 amino acids
    - (B) TYPE: AMINO ACID
    - (D) TOPOLOGY: LINEAR
  - (ii) MOLECULE TYPE: PROTEIN
  - (vi) ORIGINAL SOURCE:
    - (A) ORGANISM: Homo Sapiens
    - (F) TISSUE TYPE: Brain
  - (ix) FEATURE:
    - (A) NAME/KEY: sig\_peptide
    - (B) LOCATION: -13..-1
    - (C) IDENTIFICATION METHOD: Von Heijne matrix
    - (D) OTHER INFORMATION: score 3.5

seq MHLLSNWANPASS/RR

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 398:

Met His Leu Leu Ser Asn Trp Ala Asn Pro Ala Ser Ser Arg Arg Pro
-10 -5 1

Ser Met Ala Ala Ser Gly Thr Ser Trp Ile Ser Ser Thr Leu Ala His
5 10 15

Ser Leu Ser Leu Arg Asp Val Ser Glu Arg Leu Cys Ser Cys Trp Arg 20 25 30 35

Thr Ile Ser Met Gly Pro Cys Ala Arg Gly Ser Pro Met Asn Ser Ser 40 45 50

Gly Val His Arg Lys Ser Ser Arg Leu Phe Tyr Ile Arg Thr Pro Met
55 60 65

Arg Arg

- (2) INFORMATION FOR SEQ ID NO: 399:
  - (i) SEQUENCE CHARACTERISTICS:
    - (A) LENGTH: 118 amino acids
    - (B) TYPE: AMINO ACID
    - (D) TOPOLOGY: LINEAR
  - (ii) MOLECULE TYPE: PROTEIN
  - (vi) ORIGINAL SOURCE:
    - (A) ORGANISM: Homo Sapiens

(F) TISSUE TYPE: Brain

(ix) FEATURE:

(A) NAME/KEY: sig\_peptide

(B) LOCATION: -24..-1

- (C) IDENTIFICATION METHOD: Von Heijne matrix
- (D) OTHER INFORMATION: score 3.5 seq FAMLHSVWRLIPA/FR
- (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 399:

Met Trp Ser Gly Lys Trp Ala Leu Val Ser Pro Phe Ala Met Leu His
-20 -15 -10

Ser Val Trp Arg Leu Ile Pro Ala Phe Arg Gly Tyr Ala Gln Gln Asp -5 5

Ala Gln Glu Phe Leu Cys Glu Leu Leu Asp Lys Ile Gln Arg Glu Leu 10 20

Glu Thr Thr Gly Thr Ser Leu Pro Ala Leu Ile Pro Thr Ser Gln Arg 35 40

Lys Leu Ile Lys Gln Val Leu Asn Val Val Asn Asn Ile Phe His Gly
45 50 55

Gln Leu Leu Ser Gln Val Thr Cys Leu Ala Cys Asp Asn Lys Ser Asn 60 65 70

Thr Ile Glu Pro Phe Trp Asp Leu Ser Leu Glu Xaa Pro Glu Arg Tyr
75 80 85

Gln Cys Ser Xaa Lys Gly

- (2) INFORMATION FOR SEQ ID NO: 400:
  - (i) SEQUENCE CHARACTERISTICS:
    - (A) LENGTH: 41 amino acids
    - (B) TYPE: AMINO ACID
    - (D) TOPOLOGY: LINEAR
  - (ii) MOLECULE TYPE: PROTEIN
  - (vi) ORIGINAL SOURCE:
    - (A) ORGANISM: Homo Sapiens
    - (F) TISSUE TYPE: Brain
  - (ix) FEATURE:
    - (A) NAME/KEY: sig peptide
    - (B) LOCATION: -20..-1
    - (C) IDENTIFICATION METHOD: Von Heijne matrix
    - (D) OTHER INFORMATION: score 3.5

seq KFCLICLLTFIFH/EC

(x1) SEQUENCE DESCRIPTION: SEQ ID NO: 400:

Met Lys Val His Met His Thr Lys Phe Cys Leu Ile Cys Leu Leu Thr -20 -15 -10 -5

Phe Ile Phe His His Cys Asn His Cys His Glu Glu His Asp His Gly
1 5 10

Pro Glu Ala Leu His Arg Gln Gln Gly 15 20

- (2) INFORMATION FOR SEQ ID NO: 401:
  - (i) SEQUENCE CHARACTERISTICS:
    - (A) LENGTH: 49 amino acids
    - (B) TYPE: AMINO ACID
    - (D) TOPOLOGY: LINEAR
  - (ii) MOLECULE TYPE: PROTEIN
  - (vi) ORIGINAL SOURCE:
    - (A) ORGANISM: Homo Sapiens
    - (F) TISSUE TYPE: Brain
  - (ix) FEATURE:
    - (A) NAME/KEY: sig\_peptide
    - (B) LOCATION: -24..-1
    - (C) IDENTIFICATION METHOD: Von Heijne matrix
    - (D) OTHER INFORMATION: score 3.5 seq ALSLFYTADTSHG/SE
  - (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 401:

Met Gly Arg Arg His Trp Val Leu Thr His Ser Ala Leu Ser Leu Phe
-20 -15 -10

Tyr Thr Ala Asp Thr Ser His Gly Ser Glu Lys Pro Tyr Leu Ser Leu
-5 5

Phe Gly Arg Glu Gly Gly Arg Glu Gly Ser Asn Pro Lys Tyr Tyr Ser 10 20

Phe 25

- (2) INFORMATION FOR SEQ ID NO: 402:
  - (i) SEQUENCE CHARACTERISTICS:
    - (A) LENGTH: 93 amino acids
    - (B) TYPE: AMINO ACID
    - (D) TOPOLOGY: LINEAR
  - (ii) MOLECULE TYPE: PROTEIN
  - (vi) ORIGINAL SOURCE:
    - (A) ORGANISM: Homo Sapiens
    - (F) TISSUE TYPE: Brain

(iii) FEATURE:

(A) NAME/KEY: sig\_peptide

(B) LOCATION: -16..-1

- (C) IDENTIFICATION METHOD: Von Heijne matrix
- (D) OTHER INFORMATION: score 12.5 seq FVVLLALVAGVLG/NE

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 402:

Met Ala Val Phe Val Val Leu Leu Ala Leu Val Ala Gly Val Leu Gly

As n Glu Phe Ser Ile Leu Lys Ser Pro Gly Ser Val Val Phe Arg As n 1 5 10 15

Gly Asn Trp Pro Ile Pro Gly Glu Arg Ile Pro Asp Val Ala Ala Leu 20 25 30

Ser Met Gly Phe Ser Val Lys Glu Asp Leu Ser Trp Pro Gly Leu Ala 35 40 45

Val Gly Asn Leu Phe His Arg Pro Arg Ala Ser Val Met Val Met Val 50 60

Lys Gly Val Asn Asn Xaa Pro Leu Pro Pro Xaa Trp Xaa 65 75

- (2) INFORMATION FOR SEQ ID NO: 403:
  - (i) SEQUENCE CHARACTERISTICS:
    - (A) LENGTH: 65 amino acids
    - (B) TYPE: AMINO ACID
    - (D) TOPOLOGY: LINEAR
  - (ii) MOLECULE TYPE: PROTEIN
  - (vi) ORIGINAL SOURCE:
    - (A) ORGANISM: Homo Sapiens
    - (F) TISSUE TYPE: Brain
  - (ix) FEATURE:
    - (A) NAME/KEY: sig\_peptide
    - (B) LOCATION: -16..-1
    - (C) IDENTIFICATION METHOD: Von Heijne matrix
    - (D) OTHER INFORMATION: score 10.1

seq LLLQLAVLGAALA/AA

- (X1) SEQUENCE DESCRIPTION: SEQ ID NO: 403:
- Met Ala Pro Leu Leu Gl<br/>n Leu Gl<br/>a Val Leu Gly Ala Ala Leu Ala -15 -5
- Ala Ala Ala Lou Val Leu Ilo Ser Ilo Val Ala Phe Thr Thr Ala Thr I 5 10 15
- Lys Met Pro Ala Leu His Arg His Glu Glu Glu Lys Phe Phe Leu Asn 20 80

Ala Lys Gly Gln Lys Glu Thr Leu Pro Ser Ile Trp Asp Ser Pro Thr
35 40 45

Arg

- (2) INFORMATION FOR SEQ ID NO: 404:
  - (i) SEQUENCE CHARACTERISTICS:
    - (A) LENGTH: 84 amino acids
    - (B) TYPE: AMINO ACID
    - (D) TOPOLOGY: LINEAR
  - (ii) MOLECULE TYPE: PROTEIN
  - (vi) ORIGINAL SOURCE:
    - (A) ORGANISM: Homo Sapiens
    - (F) TISSUE TYPE: Brain
  - (ix) FEATURE:
    - · (A) NAME/KEY: sig\_peptide
      - (B) LOCATION: -50..-1
      - (C) IDENTIFICATION METHOD: Von Heijne matrix
      - (D) OTHER INFORMATION: score 9.8 seq LLRLLQLVSTCVA/FS
  - (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 404:

Met Pro Val Thr Val Thr Arg Thr Thr Ile Thr Thr Thr Thr Ser
-50 -45 -40 -35

Ser Ser Gly Leu Gly Ser Pro Met Ile Val Gly Ser Pro Arg Ala Leu
-30 -25 -20

Thr Gln Pro Leu Gly Leu Leu Arg Leu Leu Gln Leu Val Ser Thr Cys
-15 -10 -5

Val Ala Phe Ser Leu Val Ala Ser Val Gly Ala Trp Thr Gly Ser Met

Gly Asn Trp Ser Met Phe Thr Trp Cys Phe Cys Phe Ser Val Thr Leu 15 20 25 30

Ile Ile Leu Ile

- (2) INFORMATION FOR SEQ ID NO: 405:
  - (i) SEQUENCE CHARACTERISTICS:
    - (A) LENGTH: 72 amino acids
    - (B) TYPE: AMINO ACID
    - (D) TOPOLOGY: LINEAR
  - (ii) MOLECULE TYPE: PROTEIN
  - (vi) ORIGINAL SOURCE:
    - (A) ORGANISM: Homo Sapiens

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(F) TISSUE TYPE: Brain

(ix) FEATURE:

(A) NAME/KEY: sig\_peptide

(B) LOCATION: -18..-1

(C) IDENTIFICATION METHOD: Von Heijne matrix

(D) OTHER INFORMATION: score 9.2

seg VFLCSLLAPMVLA/SA

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 405:

Met Glu Leu Val Leu Val Phe Leu Cys Ser Leu Leu Ala Pro Met Val -15 -10 -5

Leu Ala Ser Ala Ala Glu Lys Glu Lys Glu Met Asp Pro Phe His Tyr
1 5 10

Asp Tyr Gln Thr Leu Arg Ile Gly Gly Leu Val Phe Ala Val Val Leu 15 20 25 30

Phe Ser Val Gly Ile Leu Leu Ile Leu Ser Arg Arg Cys Lys Cys Ser 35 40 45

Phe Asn Gln Lys Pro Arg Asn Arg 50

- (2) INFORMATION FOR SEQ ID NO: 406:
  - (i) SEQUENCE CHARACTERISTICS:
    - (A) LENGTH: 70 amino acids
    - (B) TYPE: AMINO ACID
    - (D) TOPOLOGY: LINEAR
  - (ii) MOLECULE TYPE: PROTEIN
  - (vi) ORIGINAL SOURCE:
    - (A) ORGANISM: Homo Sapiens
    - (F) TISSUE TYPE: Brain
  - (ix) FEATURE:
    - (A) NAME/KEY: sig\_peptide
    - (B) LOCATION: -46..-1
    - (C) IDENTIFICATION METHOD: Von Heijne matrix
    - (D) OTHER INFORMATION: score 7.9

seq LLGLLSAEQLAEA/SV

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 406:

Met Gly Pro Ile Trp Ser Ser Tyr Tyr Gly Asn Cys Arg Ser Leu Leu -45 -35

Fine Val Met Asp Ala Ser Asp Pro Thr Gin Leu Ser Ala  $\sim$ r Cys Val -30 -25 -20 -15

Gin Leu Leu Gly Leu Ser Ala Giu Gin Leu Ala Giu Ara Ser Val -10 -5 1 376

Leu Ile Leu Phe Asn Lys Ile Asp Leu Pro Cys Tyr Met Ser Thr Glu
5 10 15

Glu Met Lys Ser Leu Ile 20

- (2) INFORMATION FOR SEQ ID NO: 407:
  - (i) SEQUENCE CHARACTERISTICS:
    - (A) LENGTH: 57 amino acids
    - (B) TYPE: AMINO ACID
    - (D) TOPOLOGY: LINEAR
  - (ii) MOLECULE TYPE: PROTEIN
  - (vi) ORIGINAL SOURCE:
    - (A) ORGANISM: Homo Sapiens
    - (F) TISSUE TYPE: Brain
  - (ix) FEATURE:
    - (A) NAME/KEY: sig\_peptide
    - (B) LOCATION: -47..-1
    - (C) IDENTIFICATION METHOD: Von Heijne matrix
    - (D) OTHER INFORMATION: score 7.9 seq LLLPRVLLTMASG/SP
  - (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 407:
- Met Ser Gly Gly Arg Ala Pro Ala Val Leu Leu Gly Gly Val Ala Ser
  -45 -40 -35
- Leu Leu Ser Phe Val Trp Met Pro Ala Leu Leu Pro Val Ala Ser
  -30 -25 -20
- Arg Leu Leu Leu Pro Arg Val Leu Leu Thr Met Ala Ser Gly Ser -15 -5 1

Pro Pro Thr Gln Pro Ser Pro Ala Trp
5 10

- (2) INFORMATION FOR SEQ ID NO: 408:
  - (i) SEQUENCE CHARACTERISTICS:
    - (A) LENGTH: 92 amino acids
    - (B) TYPE: AMINO ACID
    - (D) TOPOLOGY: LINEAR
  - (ii) MOLECULE TYPE: PROTEIN
  - (vi) ORIGINAL SOURCE:
    - (A) ORGANISM: Homo Sapiens
    - (F) TISSUE TYPE: Brain
  - (ix) FEATURE:
    - (A) NAME/KEY: sig\_peptide
    - (3) LOCATION: -40..-1

(C) IDENTIFICATION METHOD: Von Heijne matrix

(D) OTHER INFORMATION: score 7.9 seq SLLLLFGGQFASS/QE

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 408:

Met Ala Leu Ser Cys Thr Leu Asn Arg Tyr Leu Leu Leu Met Ala Gln -35 -30 -30

Glu His Leu Glu Phe Arg Leu Pro Glu Ile Xaa Ser Leu Leu Leu -20 -15 -10

Phe Gly Gly Gln Phe Ala Ser Ser Gln Glu Thr Tyr Gly Lys Ser Pro
-5 1 5

Phe Trp Ile Leu Ser Ile Pro Ser Glu Asp Ile Ala Arg Asn Leu Met 10 20

Lys Arg Thr Val Cys Ala Lys Ser Ile Phe Glu Leu Trp Gly His Gly 25 30 35 40

Gln Ser Pro Glu Glu Leu Tyr Ser Ser Leu Lys Asn 45

# (2) INFORMATION FOR SEQ ID NO: 409:

- (i) SEQUENCE CHARACTERISTICS:
  - (A) LENGTH: 91 amino acids
  - (B) TYPE: AMINO ACID
  - (D) TOPOLOGY: LINEAR
- (ii) MOLECULE TYPE: PROTEIN
- (vi) ORIGINAL SOURCE:
  - (A) ORGANISM: Homo Sapiens
  - (F) TISSUE TYPE: Brain
- (ix) FEATURE:
  - (A) NAME/KEY: sig\_peptide
  - (B) LOCATION: -53..-1
  - (C) IDENTIFICATION METHOD: Von Heijne matrix
  - (D) OTHER INFORMATION: score 7.1

seq IAVGLGVAALAFA/GR

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 409:

Met Ala Ala Arg Gly Val Ile Ala Pro Val Gly Glu Ser Leu Arg Tyr
-50 -45

Ala Glu Tyr Leu Gln Pro Ser Ala Lys Arg Pro Asp Ala Asp Val Asp
-35
-25

Gin Gln Arg Leu Val Arg Ser Leu Ile Ala Val Gly Len Gly Val Ala

Ala Leu Ala Phe Ala Gly Arg Tyr Ala Phe Arg Ile Tro Lys Pro Leu -5 10

Glu Gln Val Ile Thr Glu Thr Ala Lys Lys Ile Ser Thr Pro Ser Phe
15 20 25

Ser Ser Tyr Tyr Lys Gly Gly Phe Glu Arg Arg
30 35

- (2) INFORMATION FOR SEQ ID NO: 410:
  - (i) SEQUENCE CHARACTERISTICS:
    - (A) LENGTH: 31 amino acids
    - (B) TYPE: AMINO ACID
    - wa (D) TOPOLOGY: LINEAR
  - (ii) MOLECULE TYPE: PROTEIN
  - (vi) ORIGINAL SOURCE:
    - (A) ORGANISM: Homo Sapiens
    - (F) TISSUE TYPE: Brain
  - (ix) FEATURE:
    - (A) NAME/KEY: sig\_peptide
    - (B) LOCATION: -28..-1
    - (C) IDENTIFICATION METHOD: Von Heijne matrix
    - (D) OTHER INFORMATION: score 6.6

seq VLGXLFLGGLCRG/WD

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 410:

Met Arg Met Cys Ala Gly Ser Ile Tyr Lys Ser Ala Thr Gln Ala Val

Leu Gly Xaa Leu Phe Leu Gly Gly Leu Cys Arg Gly Trp Asp Ala

- (2) INFORMATION FOR SEQ ID NO: 411:
  - (i) SEQUENCE CHARACTERISTICS:
    - (A) LENGTH: 80 amino acids
    - (B) TYPE: AMINO ACID
    - (D) TOPOLOGY: LINEAR
  - (ii) MOLECULE TYPE: PROTEIN
  - (vi) ORIGINAL SOURCE:
    - (A) ORGANISM: Homo Sapiens
    - (F) TISSUE TYPE: Brain
  - (ix) FEATURE:
    - (A) NAME/KEY: sig\_peptide
    - (B) LOCATION: -78..-1
    - (C) IDENTIFICATION METHOD: Von Heijne matrix
    - (D) OTHER INFORMATION: score 6.3 seq TLIMLLSWQLSVS/SV
  - (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 411:

Met Ala Glu Arg Arg Arg Pro Leu Ser Pro Ile Pro Ser Xaa Arg Arg

Pro Ser Glu Pro Ser Arg Pro Arg Pro Ala Ala Ala Gly Xaa Arg Ser
-60 -55 -50

Leu Pro Arg Pro Gly Asp Glu Glu Leu Gln Leu Pro Cys Ala Val His

Asp Leu Ile Phe Trp Arg Asp Val Lys Lys Thr Gly Phe Val Phe Gly -30 -25 -20 -15

Thr Thr Leu Ile Met Leu Leu Ser Trp Gln Leu Ser Val Ser Ser Val -10 -5 . 1

# (2) INFORMATION FOR SEQ ID NO: 412:

- (i) SEQUENCE CHARACTERISTICS:
  - (A) LENGTH: 133 amino acids
  - (B) TYPE: AMINO ACID
  - (D) TOPOLOGY: LINEAR
- (ii) MOLECULE TYPE: PROTEIN
- (vi) ORIGINAL SOURCE:
  - (A) ORGANISM: Homo Sapiens
  - (F) TISSUE TYPE: Brain
- (ix) FEATURE:
  - (A) NAME/KEY: sig\_peptide
  - (B) LOCATION: -109..-1
  - (C) IDENTIFICATION METHOD: Von Heijne matrix
  - (D) OTHER INFORMATION: score 6 seq LQLLLGMTASAVA/AL
- (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 412:

Met Ala Ala Pro Val Leu Leu Arg Val Ser Val Pro Arg Trp Glu Arg

Val Ala Arg Tyr Ala Val Cys Ala Ala Gly Ile Leu Leu Ser Ile Tyr
-80 -80

Ala Tyr His Val Glu Arg Glu Lys Glu Arg Asp Pro Glu His Arg Ala
-75 -70 -65

Leu Cys Asp leu Gly Pro Trp Val Lys Cys Ser Ala Ala Leu Ala Ser -60 -55 -50

Arg Trp Gly Arg Gly Phe Gly Lou Leu Gly Ser Ile Phe Gly Lys Asp -45 -35 -30

Gly Val Leu Ash Gln Pro Ash Ser Val Phe Gly Leu lle Phe Tyr Ile
-25 -20 -15

Leu Gin Leu Doi Leu Gly Met Thi Ala Ser Ala Val Ala Ala Leu Ile

-10 -5

Leu Met Thr Ser Ser Ile Met Ser Val Val Gly Ser Cys Thr Trp Pro
5 10 15

Thr Phe Cys Thr Thr 20

- (2) INFORMATION FOR SEQ ID NO: 413:
  - (i) SEQUENCE CHARACTERISTICS:
    - (A) LENGTH: 106 amino acids
    - (B) TYPE: AMINO ACID
    - (D) TOPOLOGY: LINEAR
  - (ii) MOLECULE TYPE: PROTEIN
  - (vi) ORIGINAL SOURCE:
    - (A) ORGANISM: Homo Sapiens
    - (F) TISSUE TYPE: Brain
  - (ix) FEATURE:
    - (A) NAME/KEY: sig\_peptide
    - (B) LOCATION: -34..-1
    - (C) IDENTIFICATION METHOD: Von Heijne matrix
    - (D) OTHER INFORMATION: score 5.9 seq LGAAALALLLANT/DV
  - (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 413:

Met Ser Phe Leu Gln Asp Pro Ser Phe Phe Thr Met Gly Met Trp Ser
-30 -25 -20

Ile Gly Ala Gly Ala Leu Gly Ala Ala Ala Leu Ala Leu Leu Leu Ala
-15
-10
-5

Asn Thr Asp Val Phe Leu Ser Lys Pro Xaa Lys Ala Ala Leu Glu Tyr

Leu Glu Asp Ile Asp Leu Lys Thr Leu Glu Lys Glu Pro Arg Thr Phe 15 20 25 30

Lys Ala Lys Glu Leu Trp Glu Lys Asn Gly Ala Val Ile Met Ala Val
35 40 45

Arg Arg Pro Gly Cys Phe Leu Cys Arg Glu Glu Ala Ala Asp Leu Ser 50 55 60

Ser Leu Lys Ser Met Leu Asp Gln Leu Gly 65 70

- (2) INFORMATION FOR SEQ ID NO: 414:
  - (i) SEQUENCE CHARACTERISTICS:
    - (A) LENGTH: 56 amino acids
    - (B) TYPE: AMINO ACID

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(D) TOPOLOGY: LINEAR

- (ii) MOLECULE TYPE: PROTEIN
- (vi) ORIGINAL SOURCE:
  - (A) ORGANISM: Homo Sapiens
  - (F) TISSUE TYPE: Brain
- (ix) FEATURE:
  - (A) NAME/KEY: sig\_peptide
  - (B) LOCATION: -37..-1
  - (C) IDENTIFICATION METHOD: Von Heijne matrix
  - (D) OTHER INFORMATION: score 4.9

seq MLIMLGIFFNVHS/AV

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 414:

Met Ala Ser Leu Leu Cys Cys Gly Pro Lys Leu Ala Ala Cys Gly Ile

Val Leu Ser Ala Trp Gly Val Ile Met Leu Ile Met Leu Gly Ile Phe

Phe Asn Val His Ser Ala Val Leu Ile Glu Asp Val Pro Phe Thr Glu -5 5 10

Lys Asp Phe Glu Asn Gly Pro Arg

- (2) INFORMATION FOR SEQ ID NO: 415:
  - (i) SEQUENCE CHARACTERISTICS:
    - (A) LENGTH: 32 amino acids
    - (B) TYPE: AMINO ACID
    - (D) TOPOLOGY: LINEAR
  - (ii) MOLECULE TYPE: PROTEIN
  - (vi) ORIGINAL SOURCE:
    - (A) ORGANISM: Homo Sapiens
    - (F) TISSUE TYPE: Brain
  - (ix) FEATURE:
    - (A) NAME/KEY: sig\_peptide
    - (B) LOCATION: -20..-1
    - (C) IDENTIFICATION METHOD: Von Heijne matrix
    - (D) OTHER INFORMATION: score 4.9

seq XSLFLHAVSSSFT/QL

(x1) SEQUENCE DESCRIPTION: SEQ ID NO: 415:

Met Ile Lou Pro Tyr Arg Met Xaa Ser Leu Phe Leu His Ala Val Ser -20 -15 -10 -5

Ser Ser Phe Thr Gln Leu Arg Ser Cys Gln Gly Asp Arg Val Trp Arg  $\frac{1}{5}$  10

- (2) INFORMATION FOR SEQ ID NO: 416:
  - (i) SEQUENCE CHARACTERISTICS:
    - (A) LENGTH: 78 amino acids
    - (B) TYPE: AMINO ACID
    - (D) TOPOLOGY: LINEAR
  - (ii) MOLECULE TYPE: PROTEIN
  - (vi) ORIGINAL SOURCE:
    - (A) ORGANISM: Homo Sapiens
    - (F) TISSUE TYPE: Brain
  - (ix) FEATURE:
    - (A) NAME/KEY: sig\_peptide
    - (B) LOCATION: -63..-1
    - (C) IDENTIFICATION METHOD: Von Heijne matrix
    - (D) OTHER INFORMATION: score 4.8 seq LYTVRALAGRAWA/AV
  - (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 416:
- Met Ala Thr Leu Val Glu Leu Pro Asp Ser Val Leu Leu Glu Ile Phe
  -60 -55 -50
- Ser Tyr Leu Pro Val Arg Asp Arg Ile Arg Ile Ser Arg Val Cys His
  -45 -40 -35
- Arg Trp Lys Arg Leu Val Asp Asp Arg Trp Leu Trp Arg His Val Asp -30 -25 -20
- Leu Thr Leu Tyr Thr Val Arg Ala Leu Ala Gly Arg Ala Trp Ala Ala
  -15 -5 1
- Val Ala Val Pro Gly Xaa Arg Arg Pro Pro Leu Pro Pro Trp
  5 10 15
- (2) INFORMATION FOR SEQ ID NO: 417:
  - (i) SEQUENCE CHARACTERISTICS:
    - (A) LENGTH: 92 amino acids
    - (B) TYPE: AMINO ACID
    - (D) TOPOLOGY: LINEAR
  - (ii) MOLECULE TYPE: PROTEIN
  - (vi) ORIGINAL SOURCE:
    - (A) ORGANISM: Homo Sapiens
    - (F) TISSUE TYPE: Brain
  - (ix) FEATURE:
    - (A) NAME/KEY: sig\_peptide
    - (B) LOCATION: -41..-1
    - (C) IDENTIFICATION METHOD: Von Heijne matrix
    - (D) OTHER INFORMATION: score 4.7

seq LFSCFCFLSHKFG/KK

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 417:

Met Lys Asn Ala Cys Ile Val Leu Pro Pro Thr Pro Pro Pro Ser Leu
-40 -35 -30

Gln Pro Ser Ala Ser Leu Leu Ala Pro Asn Arg Phe Leu Phe Ser Cys
-25 -15 -10

Phe Cys Phe Leu Ser His Lys Phe Gly Lys Lys Val Ile Tyr Phe Asn -5

Tyr Leu Ser Glu Leu His Glu His Leu Lys Tyr Asp Gln Leu Val Ile 10 15 20

Pro Pro Glu Val Leu Arg Tyr Asp Glu Lys Leu Gln Ser Leu His Glu 25 30 35

Gly Arg Thr Pro Xaa Pro Thr Lys Thr Pro Pro Gly
40 45 50

### (2) INFORMATION FOR SEQ ID NO: 418:

- (i) SEQUENCE CHARACTERISTICS:
  - (A) LENGTH: 55 amino acids
  - (B) TYPE: AMINO ACID
  - (D) TOPOLOGY: LINEAR
- (ii) MOLECULE TYPE: PROTEIN
- (vi) ORIGINAL SOURCE:
  - (A) ORGANISM: Homo Sapiens
  - (F) TISSUE TYPE: Brain
- (ix) FEATURE:
  - (A) NAME/KEY: sig\_peptide
  - (B) LOCATION: -23..-1
  - (C) IDENTIFICATION METHOD: Von Heijne matrix
  - (D) OTHER INFORMATION: score 4.6 seq PLQWSLLVAVVAG/SV
- (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 418:

Met Ala Phe Gly Leu Gln Met Phe Ile Gln Arg Lys Phe Pro Tyr Pro

Leu Gl<br/>n Trp Ser Leu Leu Val Ala Val Val Ala Gly Ser Val Val Ser<br/> -10 -5 1

Tyr Gly Val Thr Arg Val Kaa Ser Glu Lys Cys Asn Asn Leu Trp Leu 5

Phe Leu Glu Thr Gly Leu Gly

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- (2) INFORMATION FOR SEQ ID NO: 419:
  - (i) SEQUENCE CHARACTERISTICS:
    - (A) LENGTH: 69 amino acids
    - (B) TYPE: AMINO ACID
    - (D) TOPOLOGY: LINEAR
  - (ii) MOLECULE TYPE: PROTEIN
  - (vi) ORIGINAL SOURCE:
    - (A) ORGANISM: Homo Sapiens
    - (F) TISSUE TYPE: Brain
  - (ix) FEATURE:
    - (A) NAME/KEY: sig\_peptide
    - (B) LOCATION: -53..-1
    - (C) IDENTIFICATION METHOD: Von Heijne matrix
    - (D) OTHER INFORMATION: score 4.5

seq LLWTPLLSPGSLR/VI

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 419:

Met Tyr Cys Lys Ile Leu Val Leu Met Leu His Thr Glu Leu Ile Arg -45

Thr Asp Tyr Ser Ser Val Asp Gln Leu Leu Leu Asn Tyr Pro Ala Glu -30

Glu Gly Leu Gly Arg Glu Arg Ser Leu Leu Trp Thr Pro Leu Leu Ser -15

Pro Gly Ser Leu Arg Val Ile Leu Glu Ser Arg Glu Val Pro Val Ser

Leu Tro Pro Gln Thr 15

- (2) INFORMATION FOR SEQ ID NO: 420:
  - (i) SEQUENCE CHARACTERISTICS:
    - (A) LENGTH: 86 amino acids
    - (B) TYPE: AMINO ACID
    - (D) TOPOLOGY: LINEAR
  - (ii) MOLECULE TYPE: PROTEIN
  - (vi) ORIGINAL SOURCE:
    - (A) ORGANISM: Homo Sapiens
    - (F) TISSUE TYPE: Brain
  - (ix) FEATURE:
    - (A) NAME/KEY: sig\_peptide
    - (B) LOCATION: -26..-1
    - (C) IDENTIFICATION METHOD: Von Heijne matrix
    - (D) OTHER INFORMATION: score 4.5

seg ENSLIILLQGLQG/RV

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 420:

Met Ala Val Ser His Ser Val Lys Glu Arg Thr Ile Ser Glu Asn Ser
-25 -20 -15

Leu Ile Ile Leu Leu Gln Gly Leu Gln Gly Arg Val Thr Thr Val Asp -10 -5 1

Leu Arg Asp Glu Ser Val Ala His Gly Arg Ile Asp Xaa Val Asp Ala 10 15 20

Phe Met Asn Ile Arg Leu Ala Lys Val Thr Tyr Thr Asp Arg Trp Gly
25 30 35

His Gln Val Lys Leu Asp Asp Leu Phe Val Thr Gly Arg Asn Val Arg
40 45 50

Tyr Val His Ile Pro Asp 55 60

# (2) INFORMATION FOR SEQ ID NO: 421:

- (i) SEQUENCE CHARACTERISTICS:
  - (A) LENGTH: 91 amino acids
  - (B) TYPE: AMINO ACID
  - (D) TOPOLOGY: LINEAR
- (ii) MOLECULE TYPE: PROTEIN
- (vi) ORIGINAL SOURCE:
  - (A) ORGANISM: Homo Sapiens
  - (F) TISSUE TYPE: Brain
- (ix) FEATURE:
  - (A) NAME/KEY: sig\_peptide
  - (B) LOCATION: -23..-1
  - (C) IDENTIFICATION METHOD: Von Heijne matrix
  - (D) OTHER INFORMATION: score 4.4

seq QFILLGTTSVVTA/AL

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 421:

Met Glu Ser Gly Gly Arg Pro Ser Leu Cys Gln Phe Ile Leu Leu Gly

Thr Thr Ser Val Val Thr Ala Ala Leu Tyr Ser Val Tyr Arg Gln Lys -5 1 5

Ala Arg Val Ser Gln Glu Leu Lys Gly Ala Lys Lys Val His Leu Gly 10 20 25

Glu Asp Leu Lys Ser Ile Leu Ser Glu Ala Pro Gly Lys Cys Val Pro 30 35 40

Tyr Ala Val Ile Glu Gly Ala Val Arg Ser Val Lys Glu Thr Leu Asn
45 50 55

Ser Gin Phe Val Glu Asn Cys Xaa Gly Val Arg

60 65

#### (2) INFORMATION FOR SEQ ID NO: 422:

- (i) SEQUENCE CHARACTERISTICS:
  - (A) LENGTH: 142 amino acids
  - (B) TYPE: AMINO ACID
  - (D) TOPOLOGY: LINEAR
- (ii) MOLECULE TYPE: PROTEIN
- (vi) ORIGINAL SOURCE:
  - (A) ORGANISM: Homo Sapiens
  - (F) TISSUE TYPE: Brain
- (ix) FEATURE:
  - (A) NAME/KEY: sig peptide
  - (B) LOCATION: -139..-1
  - (C) IDENTIFICATION METHOD: Von Heijne matrix
  - (D) OTHER INFORMATION: score 4.3

seq GILVPHSLRQAQA/SF

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 422:

Met Ala Ala Leu Asp Leu Arg Ala Xaa Trp Ile Arg Trp Ser Cys Ser
-135 -130 -125

Cys Leu Gly Xaa Leu Xaa Gly Ala Gly Glu Thr Asn Gly Val Glu
-120 -115 -110

Arg Pro Gly Gly Gly Leu Ala Leu Ala Arg Gln Gly Ser Leu Arg
-105 -100 -95

Asp Gly Arg Gln Val Gly Arg Ala Pro Ala Val Cys Phe Pro His Gly
-90 -85 -80

Ala Pro Gly Leu Pro Pro Arg Gln Arg Xaa Xaa Gly Gly Xaa Pro Glu
-75 -65 -66

Val Gln Gly Glu Ser Trp Cys Pro Arg Pro Arg Gly Gly Gly Ala
-55 -50 -45

Ser Arg Thr Gly Leu Arg Arg Lys Gly Pro Thr Lys Thr Pro Glu
-40 -35 -30

Pro Glu Ser Ser Glu Ala Pro Gln Asp Pro Leu Asn Trp Phe Gly Ile
-25
-20
-15

Leu Val Pro His Ser Leu Arg Gln Ala Gln Ala Ser Phe Arg
-10 -5 1

#### (2) INFORMATION FOR SEQ ID NO: 423:

- (i) SEQUENCE CHARACTERISTICS:
  - (A) LENGTH: 29 amino acids
  - (B) TYPE: AMINO ACID

(D) TOPOLOGY: LINEAR

- (ii) MOLECULE TYPE: PROTEIN
- (vi) ORIGINAL SOURCE:
  - (A) ORGANISM: Homo Sapiens
  - (F) TISSUE TYPE: Brain
- (ix) FEATURE:
  - (A) NAME/KEY: sig\_peptide
  - (B) LOCATION: -21..-1
  - (C) IDENTIFICATION METHOD: Von Heijne matrix
  - (D) OTHER INFORMATION: score 4.1

seq WWISLLPSLLSIC/KV

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 423:

Met Ala Phe Leu Pro Ser Pro Ala Trp Trp Ile Ser Leu Leu Pro Ser
-20 -15 -10

Leu Leu Ser Ile Cys Lys Val Leu Met Pro Lys Leu Lys

- (2) INFORMATION FOR SEQ ID NO: 424:
  - (i) SEQUENCE CHARACTERISTICS:
    - (A) LENGTH: 127 amino acids
    - (B) TYPE: AMINO ACID
    - (D) TOPOLOGY: LINEAR
  - (ii) MOLECULE TYPE: PROTEIN
  - (vi) ORIGINAL SOURCE:
    - (A) ORGANISM: Homo Sapiens
    - (F) TISSUE TYPE: Brain
  - (ix) FEATURE:
    - (A) NAME/KEY: sig\_peptide
    - (B) LOCATION: -49..-1
    - (C) IDENTIFICATION METHOD: Von Heijne matrix
    - (D) OTHER INFORMATION: score 3.8

seq PAFHLPLPGPTLA/FL

- (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 424:
- Met Glu Pro Lys Val Ala Glu Leu Lys Gln Lys Ile Glu Asp Thr Leu
  -45 -40 -35
- Cys Pro Phe Gly Phe Glu Val Tyr Pro Phe Gln Val Ala Trp Tyr Asn  $\sim 30$  -25 -20
- Glu Leu Pro Pro Ala Phe His Leu Pro Leu Pro Gly Pro Thr Leu
  -15 -10 -5
- Ala Phe Leu Val Leu Ser Thr Pro Ala Met Phe Asp Arg Ala Leu Lys
  1 5 10

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Pro Phe Leu Gln Ser Cys His Leu Arg Met Leu Thr Asp Pro Val Asp 20 25 30

Gln Cys Val Ala Tyr His Leu Gly Arg Val Arg Glu Ser Leu Pro Glu 35 40 45

Leu Gln Ile Glu Ile Ile Ala Xaa Xaa Arg Gly Ala Pro Gln Pro Thr 50 55

Pro Gln Asp Pro Gly Pro Asp Ser Ser His Val Ala Gly Ala Ala 65 70 75

#### (2) INFORMATION FOR SEQ ID NO: 425:

- (i) SEQUENCE CHARACTERISTICS:
  - (A) LENGTH: 98 amino acids
  - (B) TYPE: AMINO ACID
  - (D) TOPOLOGY: LINEAR
- (ii) MOLECULE TYPE: PROTEIN
- (vi) ORIGINAL SOURCE:
  - (A) ORGANISM: Homo Sapiens
  - (F) TISSUE TYPE: Brain
- (ix) FEATURE:
  - (A) NAME/KEY: sig\_peptide
  - (B) LOCATION: -13..-1
  - (C) IDENTIFICATION METHOD: Von Heijne matrix
  - (D) OTHER INFORMATION: score 3.7 seq MLVLRSGLTKALA/SR

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 425:

Met Leu Val Leu Arg Ser Gly Leu Thr Lys Ala Leu Ala Ser Arg Thr
-10 -5

Leu Ala Pro Gln Val Cys Ser Ser Phe Ala Thr Gly Pro Arg Gln Tyr
5 10 15

Asp Gly Thr Phe Tyr Glu Phe Arg Thr Tyr Tyr Leu Lys Pro Ser Asn 20 25 30 35

Met Asn Ala Phe Met Glu Asn Leu Lys Lys Asn Ile His Leu Arg Thr

Ser Tyr Ser Glu Leu Val Gly Phe Trp Ser Val Glu Phe Gly Gly Arg
55 60 65

Thr Asn Lys Val Phe His Ile Trp Lys Tyr Asp Asn Phe Ala His Arg
70 75 80

Ala Glu 85

(2) INFORMATION FOR SEQ ID NO: 426:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 27 amino acids

- (B) TYPE: AMINO ACID
- (D) TOPOLOGY: LINEAR
- (ii) MOLECULE TYPE: PROTEIN
- (vi) ORIGINAL SOURCE:
  - (A) ORGANISM: Homo Sapiens
  - (F) TISSUE TYPE: Brain
- (ix) FEATURE:
  - (A) NAME/KEY: sig\_peptide
  - (B) LOCATION: -23..-1
  - (C) IDENTIFICATION METHOD: Von Heijne matrix
  - (D) OTHER INFORMATION: score 10.5 seq LLFVLLLFSLLPA/CL
- (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 426:

Met Ser Gly Gly His Leu Ala Asp Leu Thr Leu Leu Phe Val Leu Leu -20 -15 -10

Leu Phe Ser Leu Leu Pro Ala Cys Leu Pro Arg

- (2) INFORMATION FOR SEQ ID NO: 427:
  - (i) SEQUENCE CHARACTERISTICS:
    - (A) LENGTH: 54 amino acids
    - (B) TYPE: AMINO ACID
    - (D) TOPOLOGY: LINEAR
  - (ii) MOLECULE TYPE: PROTEIN
  - (vi) ORIGINAL SOURCE:
    - (A) ORGANISM: Homo Sapiens
    - (F) TISSUE TYPE: Brain
  - (ix) FEATURE:
    - (A) NAME/KEY: sig\_peptide
    - (B) LOCATION: -51..-1
    - (C) IDENTIFICATION METHOD: Von Heijne matrix
    - (D) OTHER INFORMATION: score 10.1

seq LLGALTLLGLVTS/FY

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 427:

Mct Lys Pro Ser Arg Thr Pro Ala Arg Leu Trp Met Leu Pro Gln Gln
-50 -45

Gln Ala Gly Ala Val Val Val Ala Ala Pro Thr Glu Arg His Pro Thr -35 -25 -20

His His Met Ala Gly Trp Leu Leu Gly Ala Leu Thr Leu Leu Gly Leu -15 -10 -5

Val Tnr Ser Phe Tyr Lys

- (2) INFORMATION FOR SEQ ID NO: 428:
  - (i) SEQUENCE CHARACTERISTICS:
    - (A) LENGTH: 131 amino acids
    - (B) TYPE: AMINO ACID
    - (D) TOPOLOGY: LINEAR
  - (ii) MOLECULE TYPE: PROTEIN
  - (vi) ORIGINAL SOURCE:
    - (A) ORGANISM: Homo Sapiens
    - (F) TISSUE TYPE: Brain
  - (ix) FEATURE:
    - (A) NAME/KEY: sig\_peptide
    - (B) LOCATION: -64..-1
    - (C) IDENTIFICATION METHOD: Von Heijne matrix

390

(D) OTHER INFORMATION: score 9.5

seq LSLLAALAHLAAA/EK

- (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 428:
- Met Gly Glu Ser Ile Pro Leu Ala Ala Pro Val Pro Val Glu Gln Ala
  -60 -55 -50
- Val Leu Glu Thr Phe Phe Ser His Leu Gly Ile Phe Ser Tyr Asp Lys
  -45
  -40
  -35
- Ala Lys Asp Asn Val Glu Lys Glu Arg Glu Ala Asn Lys Ser Ala Gly
  -30 -25 -20
- Gly Ser Trp Leu Ser Leu Leu Ala Ala Leu Ala His Leu Ala Ala Ala -15 -10 -5
- Glu Lys Val Tyr His Ser Leu Thr Tyr Leu Gly Gln Lys Leu Gly Gly
  1 5 10 15
- Gln Ser Phe Phe Ser Arg Lys Asp Ser Ile Arg Thr Ile Tyr Thr Ser
- Leu His Asn Glu Leu Lys Lys Val Val Thr Gly Arg Gly Ala Xaa Xaa 35 40 45
- Trp Asp Cys Ser Ser Arg Gly Arg Thr Pro Phe Pro Pro Val Arg Ala
  50 60

Ala Tyr Gly 65

- (2) INFORMATION FOR SEQ ID NO: 429:
  - (i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 86 amino acids

- (B) TYPE: AMINO ACID
- (D) TOPOLOGY: LINEAR
- (ii) MOLECULE TYPE: PROTEIN
- (vi) ORIGINAL SOURCE:
  - (A) ORGANISM: Homo Sapiens
  - (F) TISSUE TYPE: Brain
- (ix) FEATURE:
  - (A) NAME/KEY: sig\_peptide
  - (B) LOCATION: -38..-1
  - (C) IDENTIFICATION METHOD: Von Heijne matrix
  - (D) OTHER INFORMATION: score 9.3

seq QLLYLSLLSGLHG/QE

- (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 429:
- Met Gln Met Ser Tyr Ala Ile Arg Cys Ala Phe Tyr Gln Leu Leu Leu -35 -30 -25
- Ala Ala Leu Met Leu Val Ala Met Leu Gln Leu Leu Tyr Leu Ser Leu -20 -15 -10
- Leu Ser Gly Leu His Gly Gln Glu Glu Gln Asp Gln Tyr Phe Glu Phe
  -5 1 5
- Phe Pro Pro Ser Pro Arg Ser Val Asp Gln Val Lys Ala Gln Leu Arg
  15 20 25
- Thr Ala Leu Ala Ser Gly Gly Val Leu Asp Ala Ser Gly Asp Tyr Arg
- Val Tyr Arg Gly His Gly
- (2) INFORMATION FOR SEQ ID NO: 430:
  - (i) SEQUENCE CHARACTERISTICS:
    - (A) LENGTH: 26 amino acids
    - (3) TYPE: AMINO ACID
    - (D) TOPOLOGY: LINEAR
  - (11) MOLECULE TYPE: PROTEIN
  - (vi) ORIGINAL SOURCE:
    - (A) ORGANISM: Homo Sapiens
    - (F) TISSUE TYPE: Brain
  - (ix) FEATURE:
    - A) NAME/KEY: sig\_peptide
    - LOCATION: -24..-1
    - ; IDENTIFICATION METHOD: Von Heijne matrix
    - OTHER INFORMATION: score 9.1

seq LFAFHLLLSFILG/SR

(M1) UTGUENCE DESCRIPTION: SEQ ID NO: 430:

PCT/IB98/01236 WO 99/06552

Met Leu Arg Ala Glu Leu Lys Ile Ala Val Val Leu Phe Ala Phe His -15

Leu Leu Ser Phe Ile Leu Gly Ser Arg

- (2) INFORMATION FOR SEQ ID NO: 431:
  - (i) SEQUENCE CHARACTERISTICS:
    - (A) LENGTH: 76 amino acids
    - (B) TYPE: AMINO ACID
    - (D) TOPOLOGY: LINEAR
  - (ii) MOLECULE TYPE: PROTEIN
  - (vi) ORIGINAL SOURCE:
    - (A) ORGANISM: Homo Sapiens
    - (F) TISSUE TYPE: Brain
  - (ix) FEATURE:
    - (A) NAME/KEY: sig\_peptide
    - (3) LOCATION: -55..-1
    - (C) IDENTIFICATION METHOD: Von Heijne matrix
    - (D) OTHER INFORMATION: score 9

seq LLILLRTFLCSA/MI

- (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 431:
- Met Asn His Gln Gln Thr Leu Ile Gly Arg Leu Leu Cys Asp Leu His
- Gly Leu Ser Leu Ser Pro Pro Val Ala Asn Asn Val Gln Ala Leu Phe
- Arg Met Leu Thr Pro Glu Ala Tyr Ser Cys Leu Leu Ile Leu Leu Leu -20 -15
- Arg Thr Phe Leu Cys Ser Ala Met Ile Ala Asn Thr Leu His Leu Lys
- Tyr His Leu Gln Leu Ile Asp Asn Ala Cys Pro Glu 10 15
- (2) INFORMATION FOR SEQ ID NO: 432:
  - (i) SEQUENCE CHARACTERISTICS:
    - (A) LENGTH: 84 amino acids
    - (3) TYPE: AMINO ACID
    - (D) TOPOLOGY: LINEAR
  - (ii) MOLECULE TYPE: PROTEIN
  - (vi) ORIGINAL SOURCE:
    - (A) ORGANISM: Homo Sapiens

(F) TISSUE TYPE: Brain

(ix) FEATURE:

(A) NAME/KEY: sig\_peptide

(B) LOCATION: -40..-1

(C) IDENTIFICATION METHOD: Von Heijne matrix

(D) OTHER INFORMATION: score 8.6

seq LFCVLGIVLLVTG/IV

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 432:

Met Ile Ile Thr Ala Val Val Ser Ile Ser Val Thr Ile Phe Cys Phe -40 -35 -30 -25

Gln Thr Lys Val Asp Phe Thr Ser Cys Thr Gly Leu Phe Cys Val Leu -20 -15 -10

Gly Ile Val Leu Leu Val Thr Gly Ile Val Thr Ser Ile Val Leu Tyr -5 1 5

Phe Gln Tyr Val Tyr Trp Leu His Met Leu Tyr Ala Ala Leu Gly Ala 10 15 20

Ile Cys Phe Thr Leu Phe Leu Ala Tyr Asp Thr Gln Leu Val Leu Gly 25 30 35 40

Asn Arg Lys His

### (2) INFORMATION FOR SEQ ID NO: 433:

- (i) SEQUENCE CHARACTERISTICS:
  - (A) LENGTH: 89 amino acids
  - (B) TYPE: AMINO ACID
  - (D) TOPOLOGY: LINEAR
- (ii) MOLECULE TYPE: PROTEIN
- (vi) ORIGINAL SOURCE:
  - (A) ORGANISM: Homo Sapiens
  - (F) TISSUE TYPE: Brain
- (ix) FEATURE:
  - (A) NAME/KEY: sig\_peptide
  - (B) LOCATION: -65..-1
  - (C) IDENTIFICATION METHOD: Von Heijne matrix
  - (D) OTHER INFORMATION: score 8.4

seq LLWFIHLVFVVLX/LF

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 433:

Met Ala Ala Gly Gly Arg Met Glu Asp Gly Ser Leu Asp Ile Thr Gln -65 -55 -56

Ser Ile Glu Asp Asp Pro Leu Leu Asp Ala Gln Leu Leu Pro His His
-45 -40 -35

Ser Leu Gim Ala His Phe Arg Pro Arg Phe His Pro Leu Pro Thr Vol

-20

30 **-2**5

Ile Ile Val Asn Leu Leu Trp Phe Ile His Leu Val Phe Val Val Leu
-15 -10 -5

Xaa Leu Phe Asn Arg Cys Ala Leu Phe Xaa Ser Tyr Pro Lys Trp Asp 1 5 10

Xaa Cys Pro Gly Asn Tyr Thr Asn Pro

- (2) INFORMATION FOR SEO ID NO: 434:
  - (i) SEQUENCE CHARACTERISTICS:
    - (A) LENGTH: 59 amino acids
      - (B) TYPE: AMINO ACID
      - (D) TOPOLOGY: LINEAR
  - (ii) MOLECULE TYPE: PROTEIN
  - (vi) ORIGINAL SOURCE:
    - (A) ORGANISM: Homo Sapiens
    - (F) TISSUE TYPE: Brain
  - (ix) FEATURE:
    - (A) NAME/KEY: sig\_peptide
    - (B) LOCATION: -16..-1
    - (C) IDENTIFICATION METHOD: Von Heijne matrix
    - (D) OTHER INFORMATION: score 7.5 seq GCMLLFVFGFVGG/AV
  - (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 434:

Met Ser Pro Gly Cys Met Leu Leu Phe Val Phe Gly Phe Val Gly Gly -15 -5

Ala Val Val Ile Asn Ser Ala Ile Leu Val Ser Leu Ser Val Leu Leu 1 5 10 15

Leu Val His Phe Ser Ile Ser Thr Gly Val Pro Ala Leu Thr Gln Asn 20 25 30

Leu Pro Arg Ile Leu Arg Lys Glu Arg Pro Gly
35 40

- (2) INFORMATION FOR SEQ ID NO: 435:
  - (i) SEQUENCE CHARACTERISTICS:
    - (A) LENGTH: 67 amino acids
    - (3) TYPE: AMINO ACID
    - (D) TOPOLOGY: LINEAR
  - (ii) MOLECULE TYPE: PROTEIN
  - (vi) ORIGINAL SOURCE:
    - (A) ORGANISM: Homo Sapiens

(F) TISSUE TYPE: Brain

(ix) FEATURE:

- (A) NAME/KEY: sig\_peptide (B) LOCATION: -15..-1
- (C) IDENTIFICATION METHOD: Von Heijne matrix
- (D) OTHER INFORMATION: score 7.5

seq LLLGIALLAYVAS/VW

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 435:

Met Lys Leu Leu Gly Ile Ala Leu Leu Ala Tyr Val Ala Ser Val -10

Trp Gly Asn Phe Val Asn Met Arg Ser Ile Gln Glu Asn Gly Glu Leu

Lys Ile Glu Ser Lys Ile Glu Glu Met Val Glu Pro Leu Arg Glu Lys 25

Ile Arg Asp Leu Xaa Lys Ser Phe Thr Gln Lys Tyr Pro Pro Val Lys 40

Phe Leu Ser

50

- (2) INFORMATION FOR SEQ ID NO: 436:
  - (i) SEQUENCE CHARACTERISTICS:
    - (A) LENGTH: 151 amino acids
    - (B) TYPE: AMINO ACID
    - (D) TOPOLOGY: LINEAR
  - (ii) MOLECULE TYPE: PROTEIN
  - (vi) ORIGINAL SOURCE:
    - (A) ORGANISM: Homo Sapiens
    - (F) TISSUE TYPE: Brain
  - (ix) FEATURE:
    - (A) NAME/KEY: sig\_peptide
    - (B) LOCATION: -23...1
    - (C) IDENTIFICATION METHOD: Von Heijne matrix
    - (D) OTHER INFORMATION: score 7.5 seq LVLLLTLPLHLMA/LL
  - (x1) SEQUENCE DESCRIPTION: SEQ ID NO: 436:

Met Asp Ile Leu Val Pro Leu Leu Gln Leu Leu Val Leu Leu Thr

Leu Pro Leu His Leu Met Ala Leu Leu Gly Cys Trp Gln Pro Leu Cys

Lys Ser Tyr Pne Pro Tyr Leu Met Ala Val Leu Thr Pro Lys Ser Asn

Arg Lys Met Glu Ser Lys Lys Arg Glu Leu Phe Ser Gln Ile Lys Gly

Leu Thr Gly Ala Ser Gly Lys Val Ala Leu Leu Glu Leu Gly Cys Gly

Thr Gly Ala Asn Phe Gln Phe Tyr Pro Pro Gly Cys Arg Val Thr Cys

Leu Asp Pro Asn Pro His Phe Glu Lys Phe Leu Thr Lys Ser Met Ala

Glu Asn Arg His Leu Gln Tyr Glu Arg Phe Val Val Ala Pro Gly Glu

Asp Met Arg Xaa Leu Ala Asp Gly Ser Met Asp Val Val Cys Thr 110 115

Leu Val Leu Cys Ser Val Gln 125

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#### (2) INFORMATION FOR SEQ ID NO: 437:

- (i) SEQUENCE CHARACTERISTICS:
  - (A) LENGTH: 103 amino acids
  - (B) TYPE: AMINO ACID
  - (D) TOPOLOGY: LINEAR
- (ii) MOLECULE TYPE: PROTEIN
- (vi) ORIGINAL SOURCE:
  - (A) ORGANISM: Homo Sapiens
  - (F) TISSUE TYPE: Brain
- (ix) FEATURE:
  - (A) NAME/KEY: sig\_peptide
  - (B) LOCATION: -35..-1
  - (C) IDENTIFICATION METHOD: Von Heijne matrix
  - (D) OTHER INFORMATION: score 7.4

seq SLLLSLELASGSG/QG

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 437:

Met Glu Ala Ala Ser Pro Ser Asn Ser Thr Gly Val Glu Arg Xaa Ala

Asp Leu Met Asp Ala Asp Ser Leu Leu Leu Ser Leu Glu Leu Ala Ser

Gly Ser Gly Gln Gly Leu Ser Pro Asp Arg Arg Ala Ser Leu Leu Thr

Ser Leu Met Leu Val Lys Arg Asp Tyr Arg Tyr Asp Arg Val Leu Phe

Trp Gly Arg Ile Leu Gly Leu Val Ala Asp Tyr Tyr Ile Ala Gln Gly

Leu Ser Glu Asp Gln Leu Ala Pro Arg Lys Thr Leu Tyr Arg Se: Arg

Ser Arg Lys Arg Pro Ala Leu 65 •

- (2) INFORMATION FOR SEQ ID NO: 438:
  - (i) SEQUENCE CHARACTERISTICS:
    - (A) LENGTH: 70 amino acids
    - (B) TYPE: AMINO ACID
    - (D) TOPOLOGY: LINEAR
  - (ii) MOLECULE TYPE: PROTEIN
  - (vi) ORIGINAL SOURCE:
    - (A) ORGANISM: Homo Sapiens
    - (F) TISSUE TYPE: Brain
  - (ix) FEATURE:
    - (A) NAME/KEY: sig\_peptide
    - (B) LOCATION: -43..-1
    - (C) IDENTIFICATION METHOD: Von Heijne matrix
    - (D) OTHER INFORMATION: score 7.4

seq VLVKLLSSSASTS/RP

- (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 438:
- Met Ile Arg Gln Glu Arg Ser Thr Ser Tyr Gln Glu Ala Val Arg Pro
  -40 -35 -30
- Ala Leu Pro Ser Ser Lys Pro Cys Leu Leu Thr Ser Pro Ala Val Leu -25 -20 -15
- Val Lys Leu Leu Ser Ser Ser Ala Ser Thr Ser Arg Pro Pro Asp Leu
  -10 -5 1 5
- Gly His Leu Trp Gln Pro Ser Ser Ser Val Pro Leu His Arg Pro Pro 10 15 20

His Thr Ala Pro Pro Ala 25

- (2) INFORMATION FOR SEQ ID NO: 439:
  - (1) SEQUENCE CHARACTERISTICS:
    - (A) LENGTH: 113 amino acids
    - (B) TYPE: AMINO ACID
    - (D) TOPOLOGY: LINEAR
  - (ii) MOLECULE TYPE: PROTEIN
  - (vi) ORIGINAL SOURCE:
    - (A) ORGANISM: Homo Sapiens
    - (F) TISSUE TYPE: Brain

- (ix) FEATURE:
  - (A) NAME/KEY: sig peptide
  - (B) LOCATION: -41..-1
  - (C) IDENTIFICATION METHOD: Von Heijne matrix
  - (D) OTHER INFORMATION: score 7.4

seq ILPLLFGCLGVFG/LF

(xi) SEQUENCE DESCRIPTION: SEO ID NO: 439:

Met Lys Leu Ile Asp Tyr Gly Leu Ser Gly Tyr Gln Glu Glu Ser Ala
-40 -35 -30

Glu Val Lys Ala Met Asp Phe Ile Thr Ser Thr Ala Ile Leu Pro Leu -25 -15 -10

Leu Phe Gly Cys Leu Gly Val Phe Gly Leu Phe Arg Leu Leu Gln Trp
-5 1 5

Val Arg Gly Lys Ala Tyr Leu Arg Asn Ala Val Val Val Ile Thr Gly 10 15 20

Ala Thr Ser Gly Leu Gly Lys Glu Cys Ala Lys Val Phe Tyr Ala Xaa 25 30 35

Gly Ala Lys Leu Val Leu Cys Glu Xaa Glu Trp Trp Gly Leu Glu Glu 40 50 55

Leu Ile Arg Glu Leu Thr Ala Ser His Ala Thr Lys Val Gln Thr His
60 65 70

Lys

- (2) INFORMATION FOR SEQ ID NO: 440:
  - (i) SEQUENCE CHARACTERISTICS:
    - (A) LENGTH: 44 amino acids
    - (B) TYPE: AMINO ACID
    - (D) TOPOLOGY: LINEAR
  - (ii) MOLECULE TYPE: PROTEIN
  - (vi) ORIGINAL SOURCE:
    - (A) ORGANISM: Homo Sapiens
    - (F) TISSUE TYPE: Brain
  - (ix) FEATURE:
    - (A) NAME/KEY: sig\_peptide
    - (B) LOCATION: -19..-1
    - (C) IDENTIFICATION METHOD: Von Heijne matrix
    - (D) OTHER INFORMATION: score 7.4

seq PMLLRALAQAARA/GP

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 440:

Met Arg Cys Leu Thr Thr Pro Met Leu Leu Arg Ala Leu Ala Gln Ala
-15
-10
-5

Ala Arg Ala Gly Pro Pro Gly Gly Arg Ser Leu His Ser Ser Ala Val  $\frac{1}{5}$   $\frac{10}{5}$ 

Ala Ala Thr Tyr Lys Tyr Val Asn Met Gln Asp Gln
15 20 25

- (2) INFORMATION FOR SEQ ID NO: 441:
  - (i) SEQUENCE CHARACTERISTICS:
    - (A) LENGTH: 84 amino acids
    - (B) TYPE: AMINO ACID
    - (D) TOPOLOGY: LINEAR
  - (ii) MOLECULE TYPE: PROTEIN
  - (vi) ORIGINAL SOURCE:
    - (A) ORGANISM: Homo Sapiens
    - (F) TISSUE TYPE: Brain
  - (ix) FEATURE:
    - (A) NAME/KEY: sig\_peptide
    - (B) LOCATION: -67..-1
    - (C) IDENTIFICATION METHOD: Von Heijne matrix
    - (D) OTHER INFORMATION: score 7

seg IWTLLSSVIRCLC/AI

- (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 441:
- Met Ser Arg Phe Leu Asn Val Leu Arg Ser Trp Leu Val Met Val Ser
  -65 -60 -55
- Ile Ile Ala Met Gly Asn Thr Leu Gln Ser Phe Arg Asp His Thr Phe -50 -45 -40
- Leu Tyr Glu Lys Leu Tyr Thr Gly Lys Pro Asn Leu Val Asn Gly Leu -35
- Gln Ala Arg Thr Phe Gly Ile Trp Thr Leu Leu Ser Ser Val Ile Arg
- Cys Leu Cys Ala Ile Asp Ile His Asn Lys Thr Leu Tyr His Ile Thr  $\frac{1}{5}$

Leu Trp Thr Phe 15

- (2) INFORMATION FOR SEQ ID NO: 442:
  - (i) SEQUENCE CHARACTERISTICS:
    - (A) LENGTH: 29 amino acids
    - (B) TYPE: AMINO ACID
    - (D) TOPOLOGY: LINEAR
  - (ii) MOLECULE TYPE: PROTEIN
  - (vi) OBIGINAL SOURCE:

(A) ORGANISM: Homo Sapiens

(F) TISSUE TYPE: Brain

#### (ix) FEATURE:

- (A) NAME/KEY: sig\_peptide
- (B) LOCATION: -14..-1
- (C) IDENTIFICATION METHOD: Von Heijne matrix
- (D) OTHER INFORMATION: score 6.8

seq IFLTLSLDSRVSA/IR

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 442:

Met Ile Phe Leu Thr Leu Ser Leu Asp Ser Arg Val Ser Ala Ile Arg
-10 -5 1

Ser Pro Asn Phe Val Tyr Arg Ser Pro Thr Xaa His Gly
5 10 15

# (2) INFORMATION FOR SEQ ID NO: 443:

- (i) SEQUENCE CHARACTERISTICS:
  - (A) LENGTH: 101 amino acids
  - (B) TYPE: AMINO ACID
  - (D) TOPOLOGY: LINEAR
- (ii) MOLECULE TYPE: PROTEIN
- (vi) ORIGINAL SOURCE:
  - (A) ORGANISM: Homo Sapiens
  - (F) TISSUE TYPE: Brain
- (ix) FEATURE:
  - (A) NAME/KEY: sig\_peptide
  - (B) LOCATION: -29..-1
  - (C) IDENTIFICATION METHOD: Von Heijne matrix
  - (D) OTHER INFORMATION: score 6.8

seq LIFLCGAALLXVG/IW

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 443:

Met Gin Cys Phe Ser Phe Ile Lys Thr Met Met Ile Leu Phe Asn Leu
-25 -20 -15

Leu Ile Phe Leu Cys Gly Ala Ala Leu Leu Xaa Val Gly Ile Trp Val -10 -5 1

Ser Ile Asp Gly Ala Ser Phe Leu Lys Ile Phe Gly Pro Leu Ser Ser 5 10 15

Ser Ala Met Gln Phe Val Asn Val Gly Tyr Phe Leu Ile Ala Ala Gly 20 25 30 35

Val Val Phe Ala Leu Gly Phe Leu Gly Cys Tyr Xaa Ala Lys Thr 40 45 50

Glu Ser Xaa Cys Ala Leu Val Thr Phe Phe Xaa Ile Leu Leu Ile 55 60 65

PCT/IB98/01236 WO 99/06552 401

Phe Ile Ala Asp Val 7.0

(2) INFORMATION FOR SEO ID NO: 444:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 97 amino acids

(B) TYPE: AMINO ACID (D) TOPOLOGY: LINEAR

(ii) MOLECULE TYPE: PROTEIN

(vi) ORIGINAL SOURCE:

(A) ORGANISM: Homo Sapiens

(F) TISSUE TYPE: Brain

(ix) FEATURE:

(A) NAME/KEY: sig\_peptide

(B) LOCATION: -35..-1

(C) IDENTIFICATION METHOD: Von Heijne matrix

(D) OTHER INFORMATION: score 6.4 seq SACLLLCPTWTNP/QL

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 444:

Met Ala Glu Ala Ala Leu Glu Ala Val Arg Xaa Ser Tyr Glu Asn Ser

Arg Pro Leu Gln Gly Ser Ser Ala Cys Leu Leu Cys Pro Thr Trp -15 -10

Thr Asn Pro Gln Leu Arg Ser Thr Ser Thr Gly Thr Gly Ser Ala Pro

Thr Gly Arg Ala Leu Ser Ala Thr Leu Cys Ser Thr Gly Arg Pro Ser

Xaa Xaa Trp Ser Leu Pro Tyr Phe Arg Ala Thr Val Gly Ser Thr Glu 30 35

Val Ser Val Ala Val Thr Pro Asp Gly Tyr Ala Asp Ala Val Arg Xaa 50

Asp

(2) INFORMATION FOR SEQ ID NO: 445:

(1) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 34 amino acids

(E) TYPE: AMINO ACID

(D) TOPOLOGY: LINEAR

(ii) MOLECULE TYPE: PROTEIN

(v1) ORIGINAL SOURCE:

- (A) ORGANISM: Homo Sapiens
- (F) TISSUE TYPE: Brain
- (ix) FEATURE:
  - (A) NAME/KEY: sig\_peptide
  - (B) LOCATION: -19..-1
  - (C) IDENTIFICATION METHOD: Von Heijne matrix
  - (D) OTHER INFORMATION: score 6.4 seq SVFLLMVNGQVES/AQ
- (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 445:

Met Ala Thr Ala Ser Pro Ser Val Phe Leu Leu Met Val Asn Gly Gln
-15 -10 -5

Val Glu Ser Ala Gln Phe Pro Glu Tyr Asp Asp Leu Tyr Cys Lys Tyr
1 5 10

Cys Gln 15

- (2) INFORMATION FOR SEQ ID NO: 446:
  - (i) SEQUENCE CHARACTERISTICS:
    - (A) LENGTH: 36 amino acids
    - (B) TYPE: AMINO ACID
    - (D) TOPOLOGY: LINEAR
  - (ii) MOLECULE TYPE: PROTEIN
  - (vi) ORIGINAL SOURCE:
    - (A) ORGANISM: Homo Sapiens
    - (F) TISSUE TYPE: Brain
  - (ix) FEATURE:
    - (A) NAME/KEY: sig\_peptide
    - (B) LOCATION: -28..-1
    - (C) IDENTIFICATION METHOD: Von Heijne matrix
    - (D) OTHER INFORMATION: score 6

seq IGLMFLMLGCALP/IY

- (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 446:
- Met Ala Gly Ile Lys Ala Leu Ile Ser Leu Ser Phe Gly Gly Ala Ile
  -25 -20 -15
- Gly Leu Met Phe Leu Met Leu Gly Cys Ala Leu Pro Ile Tyr Asn Lys
  -10 -5 1

Tyr Trp Pro Trp

- (2) INFORMATION FOR SEQ ID NO: 447:
  - (i) SEQUENCE CHARACTERISTICS:

WO 99/06552 PCT/IB98/01236

(A) LENGTH: 39 amino acids

(B) TYPE: AMINO ACID

(D) TOPOLOGY: LINEAR

- (ii) MOLECULE TYPE: PROTEIN
- (vi) ORIGINAL SOURCE:
  - (A) ORGANISM: Homo Sapiens
  - (F) TISSUE TYPE: Brain
- (ix) FEATURE:
  - (A) NAME/KEY: sig\_peptide
  - (B) LOCATION: -17..-1
  - (C) IDENTIFICATION METHOD: Von Heijne matrix
  - (D) OTHER INFORMATION: score 5.9

seq ILLFGTLLMNAGA/VL

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 447:

Met Ile Gly Asp Ile Leu Leu Phe Gly Thr Leu Leu Met Asn Ala Gly
-15 -5

Ala Val Leu Asn Phe Lys Leu Lys Lys Lys Asp Thr Gln Gly Phe Gly 1 5 10 15

Glu Glu Ser Arg Glu Pro Trp

- (2) INFORMATION FOR SEQ ID NO: 448:
  - (i) SEQUENCE CHARACTERISTICS:
    - (A) LENGTH: 28 amino acids
    - (B) TYPE: AMINO ACID
    - (D) TOPOLOGY: LINEAR
  - (ii) MOLECULE TYPE: PROTEIN
  - (vi) ORIGINAL SOURCE:
    - (A) ORGANISM: Homo Sapiens
    - (F) TISSUE TYPE: Brain
  - (ix) FEATURE:
    - (A) NAME/KEY: sig\_peptide
    - (B) LOCATION: -16..-1
    - (C) IDENTIFICATION METHOD: Von Heijne matrix
    - (D) OTHER INFORMATION: score 5.9

seq MILTLSLFGSCIS/NF

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 448:

Met Lys Thr Met Ile Leu Thr Leu Ser Leu Phe Gly Ser Cys Ile Ser
-15 -10 -5

Ash Phe Glu Arg Tyr Met Thr Glu Arg Ser Ile Gln

- (2) INFORMATION FOR SEQ ID NO: 449:
  - (i) SEQUENCE CHARACTERISTICS:
    - (A) LENGTH: 82 amino acids
    - (B) TYPE: AMINO ACID
    - (D) TOPOLOGY: LINEAR
  - (ii) MOLECULE TYPE: PROTEIN
  - (vi) ORIGINAL SOURCE:
    - (A) ORGANISM: Homo Sapiens
    - (F) TISSUE TYPE: Brain
  - (ix) FEATURE:
    - (A) NAME/KEY: sig\_peptide
    - (B) LOCATION: -39..-1
    - (C) IDENTIFICATION METHOD: Von Heijne matrix
    - (D) OTHER INFORMATION: score 5.9

seq SVSVLSSLGIVLA/VV

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 449:

Met Asp Trp Arg Val Pro Pro Ser Xaa Xaa Asp Pro Gly His Gln Asp
-35
-30
-25

Ile Pro Leu Pro Val Thr Xaa Xaa Phe Ile Ser Val Ser Val Leu Ser -20 -15 -10

Ser Leu Gly Ile Val Leu Ala Val Val Cys Leu Ser Phe Asn Ile Tyr
-5 5

Asn Ser His Val Arg Tyr Ile Gln Asn Ser Gln Pro Asn Leu Asn Asn 10 20 25

Leu Thr Ala Val Gly Cys Ser Xaa Ala Leu Ala Ala Val Phe Pro Trp 30 35 40

Gly Ser

- (2) INFORMATION FOR SEQ ID NO: 450:
  - (i) SEQUENCE CHARACTERISTICS:
    - (A) LENGTH: 113 amino acids
    - (B) TYPE: AMINO ACID
    - (D) TOPOLOGY: LINEAR
  - (ii) MOLECULE TYPE: PROTEIN
  - (vi) ORIGINAL SOURCE:
    - (A) ORGANISM: Homo Sapiens
    - (F) TISSUE TYPE: Brain
  - (ix) FEATURE:
    - (A) NAME/KEY: sig\_peptide
    - (B) LOCATION: -16..-1
    - (C) IDENTIFICATION METHOD: Von Heijne matrix
    - (D) OTHER INFORMATION: score 5.8

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## seq AALPAWLSLQSRA/RT

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 450:

Met Ala Ala Ala Ala Leu Pro Ala Trp Leu Ser Leu Gln Ser Arg Ala
-15 -10 -5

Arg Thr Leu Arg Ala Phe Ser Thr Ala Val Tyr Ser Ala Thr Pro Val

Pro Xaa Pro Ser Leu Pro Glu Arg Thr Pro Gly Asn Glu Arg Pro Pro

Arg Arg Lys Ala Leu Pro Pro Arg Thr Glu Lys Met Ala Val Asp Gln
35 40 45

Asp Trp Pro Xaa Val Tyr Pro Val Ala Ala Pro Phe Lys Pro Ser Ala 50 55 60

Val Pro Leu Pro Val Arg Met Gly Tyr Pro Val Lys Lys Gly Val Pro 65 70 75 80

Trp Xaa Arg Arg Glu Ser Xaa Thr Phe Lys Asp Ser Asn Phe Leu His

Leu

- (2) INFORMATION FOR SEQ ID NO: 451:
  - (i) SEQUENCE CHARACTERISTICS:
    - (A) LENGTH: 29 amino acids
    - (B) TYPE: AMINO ACID
    - (D) TOPOLOGY: LINEAR
  - (ii) MOLECULE TYPE: PROTEIN
  - (vi) ORIGINAL SOURCE:
    - (A) ORGANISM: Homo Sapiens
    - (F) TISSUE TYPE: Brain
  - (ix) FEATURE:
    - (A) NAME/KEY: sig\_peptide
    - (B) LOCATION: -25..-1
    - (C) IDENTIFICATION METHOD: Von Heijne matrix
    - (D) OTHER INFORMATION: score 5.8 seq LWISACAMLLCHG/SL
  - (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 451:

Met Ala Met Val Ser Ala Met Ser Trp Val Leu Tyr Leu Trp Ile Se:
-25 -20 -15

Aia Cys Ala Met Leu Leu Cys His Gly Ser Leu Gln Arg

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- (2) INFORMATION FOR SEQ ID NO: 452:
  - (i) SEQUENCE CHARACTERISTICS:
    - (A) LENGTH: 78 amino acids
    - (B) TYPE: AMINO ACID
    - (D) TOPOLOGY: LINEAR
  - (ii) MOLECULE TYPE: PROTEIN
  - (vi) ORIGINAL SOURCE:
    - (A) ORGANISM: Homo Sapiens
    - (F) TISSUE TYPE: Brain
  - (ix) FEATURE:
    - (A) NAME/KEY: sig\_peptide
    - (B) LOCATION: -69..-1
    - (C) IDENTIFICATION METHOD: Von Heijne matrix
    - (D) OTHER INFORMATION: score 5.7

seq LCRLLCLVRLFCC/SS

- (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 452:
- Met Gly Lys Glu Trp Gly Trp Gln Glu Met Glu Asn Gly Gly Ala Ala
  -65 -60 -55
- Pro Ala Trp Gly Ala Gly Pro Pro Val His Pro Ala Pro Pro Val
  -50 -45 -40
- Glu Lys Thr Leu Ser Trp Gly Cys Gly Phe Gly Leu His Ser Gly Phe
  -35
  -30
  -25
- Gly Gly Ser Gly Gly Gly Val Gly Leu Cys Arg Leu Leu Cys Leu Val
- Arg Leu Phe Cys Cys Ser Ser Ile Leu Tyr Gln Arg Gln Gly -5 5
- (2) INFORMATION FOR SEQ ID NO: 453:
  - (i) SEQUENCE CHARACTERISTICS:
    - (A) LENGTH: 65 amino acids
    - (B) TYPE: AMINO ACID
    - (D) TOPOLOGY: LINEAR
  - (ii) MOLECULE TYPE: PROTEIN
  - (vi) ORIGINAL SOURCE:
    - (A) ORGANISM: Homo Sapiens
    - (F) TISSUE TYPE: Brain
  - (ix) FEATURE:
    - (A) NAME/KEY: sig\_peptide
    - (B) LOCATION: -21..-1
    - (C) IDENTIFICATION METHOD: Von Heijne matrix
    - (D) OTHER INFORMATION: score 5.6 seq LVLSLQFLLLSYD/LF
  - (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 453:

Met Leu Gln Thr Ser Asn Tyr Ser Leu Val Leu Ser Leu Gln Phe Leu -20 -15 -10

Leu Leu Ser Tyr Asp Leu Phe Val Asn Ser Phe Ser Glu Leu Leu Gln -5 5 10

Val Leu Phe Asn Ile Ile Ile Ile Phe Leu Met Phe Phe Asn Thr Ser 30 35 40

Arg

- (2) INFORMATION FOR SEQ ID NO: 454:
  - (i) SEQUENCE CHARACTERISTICS:
    - (A) LENGTH: 27 amino acids
    - (B) TYPE: AMINO ACID
    - (D) TOPOLOGY: LINEAR
  - (ii) MOLECULE TYPE: PROTEIN
  - (vi) ORIGINAL SOURCE:
    - (A) ORGANISM: Homo Sapiens
    - (F) TISSUE TYPE: Brain
  - (ix) FEATURE:
    - (A) NAME/KEY: sig\_peptide
    - (B) LOCATION: -24..-1
    - (C) IDENTIFICATION METHOD: Von Heijne matrix
    - (D) OTHER INFORMATION: score 5.5

seq MGVCLLIPGLATA/CI

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 454:

Met Trp Phe Glu Ile Leu Pro Gly Leu Ser Val Met Gly Val Cys Leu
-20 -15 -10

Leu Ile Pro Gly Leu Ala Thr Ala Cys Ile Arg

- (2) INFORMATION FOR SEQ ID NO: 455:
  - (i) SEQUENCE CHARACTERISTICS:
    - (A) LENGTH: 46 amino acids
    - (B) TYPE: AMINO ACID
    - (D) TOPOLOGY: LINEAR
  - (ii) MOLECULE TYPE: PROTEIN
  - (vi) ORIGINAL SOURCE:
    - (A) ORGANISM: Homo Sapiens
    - (F) TISSUE TYPE: Brain

- (ix) FEATURE:
  - (A) NAME/KEY: sig\_peptide
  - (B) LOCATION: -22..-1
  - (C) IDENTIFICATION METHOD: Von Heijne matrix
  - (D) OTHER INFORMATION: score 5.5

seq LADPLXLFPFSEG/LP

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 455:

Met Arg Pro Ser Pro Leu Ser Gly Ile Leu Ala Asp Pro Leu Xaa Leu
-20 -15 -10

Phe Pro Phe Ser Glu Gly Leu Pro Arg Arg Arg Ala Ala Ser Arg Ser
-5 1 5 10

Arg Leu Gln Thr Pro Ser Ala Arg Cys Ser Pro Arg Pro Gly
15 20

- (2) INFORMATION FOR SEQ ID NO: 456:
  - (i) SEQUENCE CHARACTERISTICS:
    - (A) LENGTH: 30 amino acids
    - (B) TYPE: AMINO ACID
    - (D) TOPOLOGY: LINEAR
  - (ii) MOLECULE TYPE: PROTEIN
  - (vi) ORIGINAL SOURCE:
    - (A) ORGANISM: Homo Sapiens
    - (F) TISSUE TYPE: Brain
  - (ix) FEATURE:
    - (A) NAME/KEY: sig\_peptide
    - (E) LOCATION: -27..-1
      - (C) IDENTIFICATION METHOD: Von Heijne matrix
      - (D) OTHER INFORMATION: score 5.4

seq SLMMAQXFIPAVA/KV

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 456:

Met Arg Glu Ser Leu Ser Xaa Arg Ser Trp His Leu Pro Ala Ser Leu -25 -20 -15

Met Met Ala Gln Xaa Phe Ile Pro Ala Val Ala Lys Val Gly -10 -5 1

- (2) INFORMATION FOR SEQ ID NO: 457:
  - (i) SEQUENCE CHARACTERISTICS:
    - (A) LENGTH: 60 amino acids
    - (B) TYPE: AMINO ACID
    - (D; TOPOLOGY: LINEAR
  - (ii) MOLECULE TYPE: PROTEIN

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(v1) ORIGINAL SOURCE:

- (A) ORGANISM: Homo Sapiens
- (F) TISSUE TYPE: Brain
- (ix) FEATURE:
  - (A) NAME/KEY: sig peptide
  - (B) LOCATION: -58..-1
  - (C) IDENTIFICATION METHOD: Von Heijne matrix
  - (D) OTHER INFORMATION: score 5.4

seq LSLHLLATRACYG/IL

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 457:

Met Ser Gly Val Val Pro Thr Ala Pro Glu Gln Pro Ala Xaa Glu Met

Glu Asn Gln Thr Lys Pro Pro Asp Pro Arg Pro Asp Ala Pro Pro Glu -35

Tyr Ser Ser His Xaa Phe Thr Arg Thr Pro Trp Lys Gln Leu Ser Leu -20

His Leu Leu Ala Thr Arg Ala Cys Tyr Gly Ile Leu

- (2) INFORMATION FOR SEQ ID NO: 458:
  - (i) SEQUENCE CHARACTERISTICS:
    - (A) LENGTH: 83 amino acids
    - (B) TYPE: AMINO ACID
    - (D) TOPOLOGY: LINEAR
  - (ii) MOLECULE TYPE: PROTEIN
  - (vi) ORIGINAL SOURCE:
    - (A) ORGANISM: Homo Sapiens
    - (F) TISSUE TYPE: Brain
  - (ix) FEATURE:
    - (A) NAME/KEY: sig\_peptide
    - (B) LOCATION: -77..-1
    - (C) IDENTIFICATION METHOD: Von Heijne matrix
    - (D) OTHER INFORMATION: score 5.3

seq TWVFTCLVFFCFG/LS

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 458:

Met Trp Arg Tyr Gln Phe Gly Trp Gly Val Ile Thr Arg Gly Pro Arg

Glu Ile Pro Phe Pro Pro Ser Leu Leu Ala Ser Glu Ser Leu Leu Pro

Pro Leu Pro Asp Leu Val Leu Thr Cys Thr Ser Leu Gly Phe Wal Thr -40 -45 -35

Arg Val Trp. Met Ser Leu Asn Leu Asn Glu Leu Ser Leu Tyr Ser Arg
-25 -20 -15

Thr Trp Val Phe Thr Cys Leu Val Phe Phe Cys Phe Gly Leu Ser Xaa -10 -5 1

Ser Leu Gly 5

- (2) INFORMATION FOR SEQ ID NO: 459:
  - (i) SEQUENCE CHARACTERISTICS:
    - (A) LENGTH: 39 amino acids
    - (B) TYPE: AMINO ACID
    - (D) TOPOLOGY: LINEAR
  - (ii) MOLECULE TYPE: PROTEIN
  - (vi) ORIGINAL SOURCE:
    - (A) ORGANISM: Homo Sapiens
    - (F) TISSUE TYPE: Brain
  - (ix) FEATURE:
    - (A) NAME/KEY: sig\_peptide
    - (B) LOCATION: -29..-1
    - (C) IDENTIFICATION METHOD: Von Heijne matrix
    - (D) OTHER INFORMATION: score 5.2 seq FFMLLGSLLPVKI/IE
  - (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 459:

Met Val Lys Leu Val Ala Lys Ile Leu Cys Met Val Gly Val Phe

Phe Phe Met Leu Gly Ser Leu Leu Pro Val Lys Ile Ile Glu Thr -10 -5 l

Asp Phe Glu Lys Ala Pro Gly

- (2) INFORMATION FOR SEQ ID NO: 460:
  - (i) SEQUENCE CHARACTERISTICS:
    - (A) LENGTH: 22 amino acids
    - (B) TYPE: AMINO ACID
    - (D) TOPOLOGY: LINEAR
  - (ii) MOLECULE TYPE: PROTEIN
  - (vi) ORIGINAL SOURCE:
    - (A) ORGANISM: Homo Sapiens
    - (F) TISSUE TYPE: Brain
  - (ix) FEATURE:
    - (A) NAME/KEY: sig\_peptide
    - (B) LOCATION: -17..-1

(C) IDENTIFICATION METHOD: Von Heijne matrix

(D) OTHER INFORMATION: score 5.2

seq IMCLIGLKANASS/ET

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 460:

Met Pro Val Ser Ile Met Cys Leu Ile Gly Leu Lys Ala Asn Ala Ser

Ser Glu Thr His Ser Gly

- (2) INFORMATION FOR SEQ ID NO: 461:
  - (i) SEQUENCE CHARACTERISTICS:
    - (A) LENGTH: 26 amino acids
    - (B) TYPE: AMINO ACID
    - (D) TOPOLOGY: LINEAR
  - (ii) MOLECULE TYPE: PROTEIN
  - (vi) ORIGINAL SOURCE:
    - (A) ORGANISM: Homo Sapiens
    - (F) TISSUE TYPE: Brain
  - (ix) FEATURE:
    - (A) NAME/KEY: sig\_peptide
    - (B) LOCATION: -17..-1
    - (C) IDENTIFICATION METHOD: Von Heijne matrix
    - (D) OTHER INFORMATION: score 5.2

seq LLYLVLEKLVSRA/FO

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 461:

Met Lys Val Ile Leu Leu Tyr Leu Val Leu Glu Lys Leu Val Ser Arg

Ala Phe Gln Asn Val Glu Ala Pro His Gly  $\frac{1}{5}$ 

- (2) INFORMATION FOR SEQ ID NO: 462:
  - (i) SEQUENCE CHARACTERISTICS:
    - (A) LENGTH: 46 amino acids
    - (B) TYPE: AMINO ACID
    - (D) TOPOLOGY: LINEAR
  - (ii) MOLECULE TYPE: PROTEIN
  - (vi) ORIGINAL SOURCE:
    - (A) ORGANISM: Homo Sapiens
    - (F) TISSUE TYPE: Brain
  - (1x) FEATURE:
    - (A) NAME/KEY: sig\_peptide

- (3) LOCATION: -19..-1
- (C) IDENTIFICATION METHOD: Von Heijne matrix
- (D) OTHER INFORMATION: score 5.1 seq LLLGGRVCXPSLA/VG
- (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 462:

Met Ala Val Thr Leu Ser Leu Leu Gly Gly Arg Val Cys Xaa Pro
-15 -10 -5

Ser Leu Ala Val Gly Ser Arg Pro Gly Gly Trp Arg Ala Gln Ala Leu
1 5 10

Leu Ala Gly Ser Arg Thr Pro Ile Pro Thr Gly Asn Arg Arg
15 20 25

- (2) INFORMATION FOR SEQ ID NO: 463:
  - (i) SEQUENCE CHARACTERISTICS:
    - (A) LENGTH: 49 amino acids
    - (3) TYPE: AMINO ACID
    - (D) TOPOLOGY: LINEAR
  - (ii) MOLECULE TYPE: PROTEIN
  - (vi) ORIGINAL SOURCE:
    - (A) ORGANISM: Homo Sapiens
    - (F) TISSUE TYPE: Brain
  - (ix) FEATURE:
    - (A) NAME/KEY: sig\_peptide.
    - (B) LOCATION: -23..-1
    - (C) IDENTIFICATION METHOD: Von Heijne matrix
    - (D) OTHER INFORMATION: score 5.1

seq LLPELGVVTPAQG/PR

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 463:

Met Leu Asn Gln Thr Ser Gly Arg Thr Ser Leu Leu Pro Glu Leu Gly
-20 -15 -10

Val Val Thr Pro Ala Gln Gly Pro Arg Arg Arg Val Trp Cys Gly His

Ser Lys Ala Lys Ala Arg Lys Ser Tyr Cys Ala Arg Ala Ile Asp Cys 10 20 25

Gln

- (2) INFORMATION FOR SEQ ID NO: 464:
  - (i) SEQUENCE CHARACTERISTICS:
    - (A) LENGTH: 135 amino acids
    - (E) TYPE: AMINO ACID
    - (C) TOPOLOGY: LINEAR

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- (ii) MOLECULE TYPE: PROTEIN
- (vi) ORIGINAL SOURCE:
  - (A) ORGANISM: Homo Sapiens
  - (F) TISSUE TYPE: Brain
- (ix) FEATURE:
  - (A) NAME/KEY: sig\_peptide
  - (B) LOCATION: -79..-1
  - (C) IDENTIFICATION METHOD: Von Heijne matrix
  - (D) OTHER INFORMATION: score 5 seq SFLGFSAPTPIQA/LT
- (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 464:

Met Thr Ser Glu Asn Leu Val Gln Thr Ala Pro Lys Lys Lys Lys Asn
-75 -70 -65

Lys Gly Lys Gly Leu Glu Pro Ser Gln Ser Thr Ala Ala Lys Val-60 -55 -50

Pro Lys Lys Ala Lys Thr Trp Ile Pro Glu Val His Asp Gln Lys Ala
-45 -40 -35

Asp Val Ser Ala Trp Lys Asp Leu Phe Val Pro Arg Pro Val Leu Arg -30 -25 -20

Ala Leu Ser Phe Leu Gly Phe Ser Ala Pro Thr Pro Ile Gln Ala Leu
-15 -5 1

Thr Leu Ala Pro Ala Ile Arg Asp Lys Leu Asp Ile Leu Gly Ala Ala 10 15

Glu Thr Gly Ser Gly Lys Thr Leu Ala Phe Ala Ile Pro Met Ile His 20 25 30

Ala Val Leu Gln Trp Gln Lys Arg Asn Ala Ala Pro Pro Pro Ser Asn 35 40 45

Thr Glu Ala Pro Pro Gly Glu 50 55

- (2) INFORMATION FOR SEQ ID NO: 465:
  - (i) SEQUENCE CHARACTERISTICS:
    - (A) LENGTH: 79 amino acids
    - (B) TYPE: AMINO ACID(D) TOPOLOGY: LINEAR
  - (ii) MOLECULE TYPE: PROTEIN
  - (vi) ORIGINAL SOURCE:
    - (A) ORGANISM: Homo Sapiens
    - (F) TISSUE TYPE: Brain
  - (ix) FEATURE:
    - (A) NAME/KEY: sig\_peptide

- (B) LOCATION: -23..-1
- (C) IDENTIFICATION METHOD: Von Heijne matrix
- (D) OTHER INFORMATION: score 4.9 seq WHXLIPLTWACMA/RQ
- (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 465:

Met Ala Ala Phe Gly Arg Gln Xaa Xaa Xaa Trp His Xaa Leu Ile Pro
-20 -15 -10

Leu Thr Trp Ala Cys Met Ala Arg Gln Thr Pro His Leu Gly Glu Gln -5 1 5

Arg Arg Thr Thr Ala Ser Leu Xaa Arg Lys Leu Thr Thr Ala Ser Asn
10 20 25

Gly Gly Val Ile Glu Glu Leu Ser Cys Val Arg Ser Asn Asn Tyr Val 30 35 40

Gln Glu Pro Glu Cys Arg Arg Asn Leu Val Gln Cys Leu Leu Trp 45 50 55

- (2) INFORMATION FOR SEQ ID NO: 466:
  - (i) SEQUENCE CHARACTERISTICS:
    - (A) LENGTH: 68 amino acids
    - (B) TYPE: AMINO ACID
    - (D) TOPOLOGY: LINEAR
  - (ii) MOLECULE TYPE: PROTEIN
  - (vi) ORIGINAL SOURCE:
    - (A) ORGANISM: Homo Sapiens
    - (F) TISSUE TYPE: Brain
  - (ix) FEATURE:
    - (A) NAME/KEY: sig\_peptide
    - (B) LOCATION: -57..-1
    - (C) IDENTIFICATION METHOD: Von Heijne matrix
    - (D) OTHER INFORMATION: score 4.9

seq GWFLSGCPHGSSA/TW

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 466:

Met Ser Leu Thr Ser Ser Pro Lys Lys Arg Arg Ser Ile Cys Phe Asp
-55 -50 -45

Arg Phe Leu Met Pro Gln Ser Gln Ser Gly Pro Ser Ser Leu Gly Glu
-40 -35 -30

Ser Tyr Arg Thr Gly Val Gly Phe Leu Ile Pro Glu Gly Trp Phe Leu -25 -15 -10

Ser Gly Cys Pro His Gly Ser Ser Ala Thr Trp Thr Lys Cys Gln Thr -5 1 5

Ser Ala Ser Leu

10

(2) INFORMATION FOR SEQ ID NO: 467:

- (i) SEQUENCE CHARACTERISTICS:
  - (A) LENGTH: 46 amino acids
  - (B) TYPE: AMINO ACID
  - (D) TOPOLOGY: LINEAR
- (ii) MOLECULE TYPE: PROTEIN
- (vi) ORIGINAL SOURCE:
  - (A) ORGANISM: Homo Sapiens
  - (F) TISSUE TYPE: Brain
- (ix) FEATURE:
  - (A) NAME/KEY: sig\_peptide
  - (B) LOCATION: -39..-1
  - (C) IDENTIFICATION METHOD: Von Heijne matrix
  - (D) OTHER INFORMATION: score 4.8 seq SLXFCLSPPPSPS/LR
- (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 467:

Met Gly Glu Leu Gly Asn Arg Ser Arg Cys Ile Leu Phe Leu Ser Glu
-35 -30 -25

Asn Pro Cys Leu Ser Glu Ser Ile Phe Gln Ser Leu Xaa Phe Cys Leu -20 -15 -10

Ser Pro Pro Pro Ser Pro Ser Leu Arg Pro Ser Pro Ser Arg -5 1

- (2) INFORMATION FOR SEQ ID NO: 468:
  - (i) SEQUENCE CHARACTERISTICS:
    - (A) LENGTH: 111 amino acids
    - (B) TYPE: AMINO ACID
    - (D) TOPOLOGY: LINEAR
  - (ii) MOLECULE TYPE: PROTEIN
  - (vi) ORIGINAL SOURCE:
    - (A) ORGANISM: Homo Sapiens
    - (F) TISSUE TYPE: Brain
  - (ix) FEATURE:
    - (A) NAME/KEY: sig\_peptide
    - (B) LOCATION: -93..-1
    - (C) IDENTIFICATION METHOD: Von Heijne matrix
    - (D) OTHER INFORMATION: score 4.7

seq VLLLRQXFAQAEK/WY

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 468:

Met Ala Glu Leu Gly Leu Asn Glu His His Gln Asn Glu Val Ile Asn
-90
-85
-80

Tyr Met Arg Phe Ala Arg Ser Lys Arg Gly Leu Arg Leu Lys Thr Val -75 -70 -65

Asp Ser Cys Phe Gln Asp Leu Lys Glu Ser Arg Leu Val Glu Asp Thr
-60 -55 -50

Phe Thr Ile Asp Glu Val Ser Glu Val Leu Asn Gly Leu Gln Ala Val
-45 -35 -30

Val His Ser Glu Val Glu Ser Glu Leu Ile Asn Thr Ala Tyr Thr Asn
-25
-20
-15

Val Leu Leu Arg Gln Xaa Phe Ala Gln Ala Glu Lys Trp Tyr Leu -10 -5 l

Lys Leu Gln Thr Asp Ile Ser Glu Leu Glu Asn Arg Glu Leu Leu
5 10 15

### (2) INFORMATION FOR SEO ID NO: 469:

- (i) SEQUENCE CHARACTERISTICS:
  - (A) LENGTH: 70 amino acids
  - (B) TYPE: AMINO ACID
  - (D) TOPOLOGY: LINEAR
- (ii) MOLECULE TYPE: PROTEIN
- (vi) ORIGINAL SOURCE:
  - (A) ORGANISM: Homo Sapiens
  - (F) TISSUE TYPE: Brain
- (ix) FEATURE:
  - ... (A) NAME/KEY: sig\_peptide
    - (B) LOCATION: -49..-1
    - (C) IDENTIFICATION METHOD: Von Heijne matrix
    - (D) OTHER INFORMATION: score 4.6

seq SWAVGLLYAVAQG/SK

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 469:

Met Val Thr Leu Pro Ser Gly Thr Trp Ala Phe Ser Cys Pro Tyr Leu

Ala Leu Val Asp Gly Gly Met Leu Gly Ser Ala Arg Glu Asp Ala His
-30 -25 -20

Ala Ser Val Val Ser Trp Ala Val Gly Leu Leu Tyr Ala Val Ala Gln
-15 -5

Gly Ser Lys Arg Arg Lys Val Gln Asp Val Lys Pro Leu Xaa Trp Ser 1 5 10 15

Arg Thr Gly Thr Leu Gly

- (2) INFORMATION FOR SEQ ID NO: 470:
  - (i) SEQUENCE CHARACTERISTICS:
    - (A) LENGTH: 80 amino acids
    - (B) TYPE: AMINO ACID
    - (D) TOPOLOGY: LINEAR
  - (ii) MOLECULE TYPE: PROTEIN
  - (vi) ORIGINAL SOURCE:
    - (A) ORGANISM: Homo Sapiens
    - (F) TISSUE TYPE: Brain
  - (ix) FEATURE:
    - (A) NAME/KEY: sig\_peptide
    - (B) LOCATION: -68..-1
    - (C) IDENTIFICATION METHOD: Von Heijne matrix
    - (D) OTHER INFORMATION: score 4.6

seq LPFSLVSMLVTQG/LV

- (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 470:
- Met Ala Ser Ala Ser Ala Arg Gly Asn Gln Asp Lys Asp Ala His Phe
  -65
  -60
  -55
- Pro Pro Pro Ser Lys Gln Ser Leu Leu Phe Cys Pro Lys Xaa Xaa Leu -50 -45 -40
- His Ile His Arg Ala Glu Ile Ser Lys Ile Met Arg Glu Cys Gln Glu
  -35 -25
- Glu Ser Phe Trp Lys Arg Ala Leu Pro Phe Ser Leu Val Ser Met Leu -20 -15 -10
- Val Thr Gln Gly Leu Val Tyr Gln Gly Tyr Leu Ala Ala Asn Ser Arg  $1 \hspace{1cm} 5 \hspace{1cm} 10$
- (2) INFORMATION FOR SEQ ID NO: 471:
  - (i) SEQUENCE CHARACTERISTICS:
    - (A) LENGTH: 71 amino acids
    - (B) TYPE: AMINO ACID
    - (D) TOPOLOGY: LINEAR
  - (ii) MOLECULE TYPE: PROTEIN
  - (vi) ORIGINAL SOURCE:
    - (A) ORGANISM: Homo Sapiens
    - (F) TISSUE TYPE: Brain
  - (ix) FEATURE:
    - (A) NAME/KEY: sig\_peptide
    - (B) LOCATION: -69..-1
    - (C) IDENTIFICATION METHOD: Von Heijne matrix
    - (D) OTHER INFORMATION: score 4.5
      seq FILSLGVICIVLT/TG

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(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 471:

Met Leu Met Lys Ser Ile Leu Leu Lys Val Val Cys Val Leu Cys
-65 -60 -55

Ile Tyr Leu Lys Phe Lys Leu Met Ala Leu Ile Tyr Val Pro Asp Lys
-50
-45
-40

Asn Asn Thr Asn Asn Asn Ile Leu Arg Tyr Asn His Asn Glu Ile Ser
-35 -30 -25

Ile Gly Ile Ser Val Gln Cys His Phe Ile Leu Ser Leu Cys Val Leu
-20 -15 -10

Cys Ile Val Leu Thr Thr Gly

- (2) INFORMATION FOR SEQ ID NO: 472:
  - (i) SEQUENCE CHARACTERISTICS:
    - (A) LENGTH: 50 amino acids
    - (B) TYPE: AMINO ACID
    - (D) TOPOLOGY: LINEAR
  - (ii) MOLECULE TYPE: PROTEIN
  - (vi) ORIGINAL SOURCE:
    - (A) ORGANISM: Homo Sapiens
    - (F) TISSUE TYPE: Brain
  - (ix) FEATURE:
    - (A) NAME/KEY: sig\_peptide
    - (B) LOCATION: -16..-1
    - (C) IDENTIFICATION METHOD: Von Heijne matrix
    - (D) OTHER INFORMATION: score 4.5 seq RLLLRRFLASVIS/RK
  - (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 472:

Met Ala Gln Arg Leu Leu Arg Arg Phe Leu Ala Ser Val Ile Ser

Arg Lys Pro Ser Gln Gly Gln Trp Pro Pro Leu Thr Ser Arg Ala Leu 1 5 10

Gln Thr Pro Xaa Cys Ser Xaa Gly Gly Leu Thr Val Thr Pro Asn Pro 20 25 30

Ser Arg

- (2) INFORMATION FOR SEQ ID NO: 473:
  - (i) SEQUENCE CHARACTERISTICS:
    - (A) LENGTH: 103 amino acids

(B) TYPE: AMINO ACID
(D) TOPOLOGY: LINEAR

(b) TOFOLOGI. LINEAR

- (ii) MOLECULE TYPE: PROTEIN
- (vi) ORIGINAL SOURCE:
  - (A) ORGANISM: Homo Sapiens
  - (F) TISSUE TYPE: Brain
- (ix) FEATURE:
  - (A) NAME/KEY: sig\_peptide
  - (B) LOCATION: -77..-1
  - (C) IDENTIFICATION METHOD: Von Heijne matrix
  - (D) OTHER INFORMATION: score 4.4

seg FEARIALLPLLOA/ET

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 473:

Met Ala Ala Ser Lys Val Lys Gln Asp Met Pro Pro Xaa Gly Gly Tyr
-75 -70 -65

Gly Pro Ile Asp Tyr Lys Arg Asn Leu Pro Arg Arg Gly Leu Ser Gly
-60 -55 -50

Tyr Ser Met Leu Ala Ile Gly Ile Gly Thr Leu Ile Tyr Gly His Trp
-45 -35 -30

Ser Ile Met Lys Trp Asn Arg Glu Arg Arg Arg Leu Gln Ile Glu Asp
-25 -20 -15

Phe Glu Ala Arg Ile Ala Leu Leu Pro Leu Leu Gln Ala Glu Thr Asp

Arg Arg Thr Leu Gln Met Leu Arg Glu Asn Leu Glu Glu Glu Ala Ile

Ile Met Lys Asp Val Pro Gly

- (2) INFORMATION FOR SEQ ID NO: 474:
  - (i) SEQUENCE CHARACTERISTICS:
    - (A) LENGTH: 77 amino acids
    - (B) TYPE: AMINO ACID
    - (D) TOPOLOGY: LINEAR
  - (ii) MOLECULE TYPE: PROTEIN
  - (vi) ORIGINAL SOURCE:
    - (A) ORGANISM: Homo Sapiens
    - (F) TISSUE TYPE: Brain
  - (1x) FEATURE:
    - (A) NAME/KEY: sig\_peptide
    - (B) LOCATION: -54..-1
    - (C) IDENTIFICATION METHOD: Von Heijne matrix
    - (D) OTHER INFORMATION: score 4.3

seq LLSLAILSHISTP/GC

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 474:

Met Arg His Leu Val Thr Glu Glu Leu Phe Pro Cys Ser Asn Leu Glu
-50 -45 -40

Asp Val Val Glu Asp Asn Ser His Ser Tyr Phe Thr Leu Arg Ile Thr
-35
-30
-25

Met Ala Cys Lys Gly Val Pro Ser Thr Leu Leu Ser Leu Ala Ile Leu
-20 -15 -10

Ser His Ile Ser Thr Pro Gly Cys Glu Trp His Val Ile Tyr Val Ser
-5 5 10

Ser Xaa Gly Leu Tyr Leu Val Val Glu Met Thr Asp Arg 15 20

- (2) INFORMATION FOR SEQ ID NO: 475:
  - (i) SEQUENCE CHARACTERISTICS:
    - (A) LENGTH: 80 amino acids
    - (B) TYPE: AMINO ACID
    - (D) TOPOLOGY: LINEAR
  - (ii) MOLECULE TYPE: PROTEIN
  - (vi) ORIGINAL SOURCE:
    - (A) ORGANISM: Homo Sapiens
    - (F) TISSUE TYPE: Brain
  - (ix) FEATURE:
    - (A) NAME/KEY: sig\_peptide
    - (B) LOCATION: -76..-1
    - (C) IDENTIFICATION METHOD: Von Heijne matrix
    - (D) OTHER INFORMATION: score 4.3 seq FRLLXVFAYGTYA/DY
  - (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 475:

Met Ser Ala Glu Val Lys Val Thr Gly Gln Asn Gln Glu Gln Phe Leu

Leu Leu Ala Lys Ser Ala Lys Gly Ala Ala Leu Ala Thr Leu Ile His -60 -55 -50 -45

Glm Val Leu Glu Ala Pro Gly Val Tyr Val Phe Gly Glu Leu Leu Asp
-40 -35 -30

Met Pro Asn Val Arg Glu Leu Ala Glu Ser Xaa Phe Ala Ser Thr Phe
-25
-20
-15

Arg Leu Leu Xaa Val Phe Ala Tyr Gly Thr Tyr Ala Asp Tyr Xaa Ala -10 -5 1

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(2) INFORMATION FOR SEQ ID NO: 476:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 45 amino acids
- (B) TYPE: AMINO ACID
- (D) TOPOLOGY: LINEAR
- (ii) MOLECULE TYPE: PROTEIN
- (vi) ORIGINAL SOURCE:
  - (A) ORGANISM: Homo Sapiens
  - (F) TISSUE TYPE: Brain
- (ix) FEATURE:
  - (A) NAME/KEY: sig\_peptide
  - (B) LOCATION: -34..-1
  - (C) IDENTIFICATION METHOD: Von Heijne matrix
  - (D) OTHER INFORMATION: score 4.3 seq QLFAFLNLLPVEA/DI
- (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 476:

Met Leu Leu Ser Ile Gly Met Leu Met Leu Ser Ala Thr Gln Val Xaa -25

Thr Ile Leu Xaa Val Gln Leu Phe Ala Phe Leu Asn Leu Leu Pro Val -15

Glu Ala Asp Ile Xaa Ala Tyr Asn Phe Glu Asn Ala Ser

- (2) INFORMATION FOR SEQ ID NO: 477:
  - (i) SEQUENCE CHARACTERISTICS:
    - (A) LENGTH: 28 amino acids
    - (B) TYPE: AMINO ACID
    - (D) TOPOLOGY: LINEAR
  - (ii) MOLECULE TYPE: PROTEIN
  - (vi) ORIGINAL SOURCE:
    - (A) ORGANISM: Homo Sapiens
    - (F) TISSUE TYPE: Brain
  - (1x) FEATURE:
    - (A) NAME/KEY: sig\_peptide
    - (B) LOCATION: -16..-1
    - (C) IDENTIFICATION METHOD: Von Heijne matrix
    - (D) OTHER INFORMATION: score 4.2

seq EVVSLSYCGVSWG/RI

(M1) SEQUENCE DESCRIPTION: SEQ ID NO: 477:

Met Gly Trp Glu Val Val Ser Leu Ser Tyr Cys Gly Val Ser Trp Gly -10

Arg Ills for Pro Asn Leu Asn Lys Pro Val Asn Arg

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1 5 10

(2) INFORMATION FOR SEQ ID NO: 478:

- (i) SEQUENCE CHARACTERISTICS:
  - (A) LENGTH: 72 amino acids
  - (B) TYPE: AMINO ACID
  - (D) TOPOLOGY: LINEAR
- (ii) MOLECULE TYPE: PROTEIN
- (vi) ORIGINAL SOURCE:
  - (A) ORGANISM: Homo Sapiens
  - (F) TISSUE TYPE: Brain
- (ix) FEATURE:
  - (A) NAME/KEY: sig\_peptide
  - (B) LOCATION: -32..-1
  - (C) IDENTIFICATION METHOD: Von Heijne matrix
  - (D) OTHER INFORMATION: score 4.2

seq CWELFCLEHGIQA/DG

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 478:

Met Arg Glu Cys Ile Ser Val His Val Gly Gln Ala Gly Val Gln Ile
-30 -25 -20

Gly Asn Ala Cys Trp Glu Leu Phe Cys Leu Glu His Gly Ile Gln Ala
-15 -5

Asp Gly Thr Phe Asp Ala Gln Ala Ser Lys Ile Asn Asp Asp Ser 1 5 10 15

Phe Thr Thr Phe Phe Ser Glu Thr Gly Thr Ser Leu Leu Met Glu Arg
20 25 30

Leu Xaa Leu Asp Tyr Gly Lys Lys 35 40

- (2) INFORMATION FOR SEQ ID NO: 479:
  - (i) SEQUENCE CHARACTERISTICS:
    - (A) LENGTH: 46 amino acids
    - (B) TYPE: AMINO ACID
    - (D) TOPOLOGY: LINEAR
  - (ii) MOLECULE TYPE: PROTEIN
  - (vi) ORIGINAL SOURCE:
    - (A) ORGANISM: Homo Sapiens
    - (F) TISSUE TYPE: Brain
  - (ix) FEATURE:
    - (A) NAME/KEY: sig\_peptide
    - (B) LOCATION: -25..-1
    - (C) IDENTIFICATION METHOD: Von Heijne matrix

(D) OTHER INFORMATION: score 4.2 seq LDLLRGLPRVSLA/NL

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 479:

Met Ala Gly Pro Leu Gln Gly Gly Gly Ala Arg Ala Leu Asp Leu Leu -25 ~15

Arg Gly Leu Pro Arg Val Ser Leu Ala Asn Leu Lys Pro Asn Pro Gly

Ser Lys Lys Pro Glu Arg Arg Pro Arg Gly Arg Arg Trp 10 15

- (2) INFORMATION FOR SEQ ID NO: 480:
  - (i) SEQUENCE CHARACTERISTICS:
    - (A) LENGTH: 68 amino acids
    - (B) TYPE: AMINO ACID
    - (D) TOPOLOGY: LINEAR
  - (ii) MOLECULE TYPE: PROTEIN
  - (vi) ORIGINAL SOURCE:
    - (A) ORGANISM: Homo Sapiens
    - (F) TISSUE TYPE: Brain
  - (ix) FEATURE:
    - (A) NAME/KEY: sig\_peptide
    - (B) LOCATION: -25..-1
    - (C) IDENTIFICATION METHOD: Von Heijne matrix
    - (D) OTHER INFORMATION: score 4.2

seq MFAASXLAMCAGA/EV

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 480:

Met Pro Ala Gly Val Pro Met Ser Thr Tyr Leu Lys Met Phe Ala Ala -15

Ser Xaa Leu Ala Met Cys Ala Gly Ala Glu Val Val His Arg Tyr Tyr

Arg Pro Asp Leu Thr Ile Pro Glu Ile Pro Pro Lys Arg Gly Glu Leu

Lys Thr Glu Leu Leu Gly Leu Lys Glu Arg Lys His Lys Pro Gln Val

Ser Gln Gln Glu 40

- (2) INFORMATION FOR SEQ ID NO: 481:
  - (i) SEQUENCE CHARACTERISTICS:
    - (A) LENGTH: 32 amino acids

(B) TYPE: AMINO ACID

(D) TOPOLOGY: LINEAR

- (ii) MOLECULE TYPE: PROTEIN
- (vi) ORIGINAL SOURCE:
  - (A) ORGANISM: Homo Sapiens
  - (F) TISSUE TYPE: Brain
- (ix) FEATURE:
  - (A) NAME/KEY: sig\_peptide
  - (B) LOCATION: -24..-1
  - (C) IDENTIFICATION METHOD: Von Heijne matrix
  - (D) OTHER INFORMATION: score 4.2 seq SLPALALSLRASP/RX
- (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 481:

Met Ala Val Gln Cys Val Arg Leu Ala Arg Arg Ser Leu Pro Ala Leu
-20 -15 -10

Ala Leu Ser Leu Arg Ala Ser Pro Arg Xaa Leu Cys Thr Ala Thr Lys
-5 1 5

Gln Lys Asn Ser Gly Gln Asn Leu Glu Glu Asp Met Gly Gln Ser Glu 10 20

Gln Lys Ala Asp Pro Pro Ala Thr Glu Lys Thr Leu Leu Glu Glu Lys 25 30 35 40

Val Lys Leu Glu Glu Glu Lys Glu Thr Val Glu Lys Tyr Lys Arg 45 50 55

Ala Arg

- (2) INFORMATION FOR SEQ ID NO: 482:
  - (i) SEQUENCE CHARACTERISTICS:
    - (A) LENGTH: 42 amino acids
    - (B) TYPE: AMINO ACID
    - (D) TOPOLOGY: LINEAR
  - (ii) MOLECULE TYPE: PROTEIN
  - (vi) ORIGINAL SOURCE:
    - (A) ORGANISM: Homo Sapiens
    - (F) TISSUE TYPE: Brain
  - (ix) FEATURE:
    - (A) NAME/KEY: sig\_peptide
    - (B) LOCATION: -37..-1
    - (C) IDENTIFICATION METHOD: Von Heijne matrix
    - (D) OTHER INFORMATION: score 4.2
      - seq RLMHHYLSTPTSA/RP
  - (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 482:

Met Phe Ser Ile Ile Ser Arg Ser Arg Ala Cys Ser Met Tyr Phe Lys -35 -30 +25

Glu Asn Ala Lys Pro Ser Gln Leu Arg Leu Met His His Tyr Leu Ser -20 -15

Thr Pro Thr Ser Ala Arg Pro His His Leu -5 5

- (2) INFORMATION FOR SEQ ID NO: 483:
  - (i) SEQUENCE CHARACTERISTICS:
    - (A) LENGTH: 35 amino acids
    - (B) TYPE: AMINO ACID
    - (D) TOPOLOGY: LINEAR
  - (ii) MOLECULE TYPE: PROTEIN
  - (vi) ORIGINAL SOURCE:
    - (A) ORGANISM: Homo Sapiens
    - (F) TISSUE TYPE: Brain
  - (ix) FEATURE:
    - (A) NAME/KEY: sig\_peptide
    - (B) LOCATION: -16..-1
    - (C) IDENTIFICATION METHOD: Von Heijne matrix
    - (D) OTHER INFORMATION: score 4.1

seq LLPATSLAGPVLS/TL

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 483:

Met Lys Arg Leu Leu Pro Ala Thr Ser Leu Ala Gly Pro Val Leu Ser -15 -5

Thr Let Ile Ala Pro Thr Pro Met Let Phe Cys Glu Asp Lys Ser Trp

1 10 15

Asp Pro Gly

- (2) INFORMATION FOR SEQ ID NO: 484:
  - (i) SEQUENCE CHARACTERISTICS:
    - (A) LENGTH: 98 amino acids
    - (B) TYPE: AMINO ACID
    - (D) TOPOLOGY: LINEAR
  - (ii) MOLECULE TYPE: PROTEIN
  - (vi) ORIGINAL SOURCE:
    - (A) ORGANISM: Homo Sapiens
    - (F) TISSUE TYPE: Brain
  - (1K) FEATURE:
    - (A) NAME/KEY: sig\_peptide
    - (B) LOCATION: -70..-1
    - (C) IDENTIFICATION METHOD: Von Hoijne matrix

(D) OTHER INFORMATION: score 4

seq IAVLYLHLYDVFG/DP

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 484:

Met Leu Ile Ile Thr Asn Pro Trp Pro Lys Tyr Phe Asp Ala Ala Gly
-70
-65
-60
-55

Arg Leu Thr Pro Glu Phe Ser Gln Arg Leu Thr Asn Lys Ile Arg Glu -50 -45 -40

Leu Leu Gln Gln Met Glu Arg Gly Leu Lys Ser Ala Asp Xaa Xaa Asp
-35
-30
-25

Gly Thr Gly Tyr Thr Gly Trp Ala Gly Ile Ala Val Leu Tyr Leu His
-20 -15 -10

Leu Tyr Asp Val Phe Gly Asp Pro Ala Tyr Leu Gln Leu Ala His Gly
-5 5 10

Tyr Val Lys Gln Ser Leu Asn Cys Leu Thr Lys Arg Ser Ile Thr Phe
15 20 25

Gln Gly

- (2) INFORMATION FOR SEQ ID NO: 485:
  - (i) SEQUENCE CHARACTERISTICS:
    - (A) LENGTH: 47 amino acids
    - (B) TYPE: AMINO ACID
    - (D) TOPOLOGY: LINEAR
  - (ii) MOLECULE TYPE: PROTEIN
  - (vi) ORIGINAL SOURCE:
    - (A) ORGANISM: Homo Sapiens
    - (F) TISSUE TYPE: Brain
  - (ix) FEATURE:
    - (A) NAME/KEY: sig\_peptide.
    - (B) LOCATION: -21..-1
    - (C) IDENTIFICATION METHOD: Von Heijne matrix
    - (D) OTHER INFORMATION: score 3.9

seq AWLAQGSSSAGWG/LE

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 485:

Met Cys Ala Thr Glu Thr Val Arg Ala Tro Leu Ala Gln Gly Ser Ser -20 -15 -10

Ser Ala Gly Trp Gly Leu Glu Arg Lys Gln Gly Val Ser Ala His Arg
-5 1 5 10

Met Pro Ala Leu Arg Trp Leu Gln Lys Ser Val Pro Gly Xaa Met 15 20 25 (2) INFORMATION FOR SEQ ID NO: 486: (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 48 amino acids (B) TYPE: AMINO ACID (D) TOPOLOGY: LINEAR (11) MOLECULE TYPE: PROTEIN (vi) ORIGINAL SOURCE: (A) ORGANISM: Homo Sapiens (F) TISSUE TYPE: Brain (ix) FEATURE: (A) NAME/KEY: sig\_peptide (B) LOCATION: -46..-1 (C) IDENTIFICATION METHOD: Von Heijne matrix (D) OTHER INFORMATION: score 3.9 seq AAAFCLKXXGANT/HP (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 486: Met Leu Leu Leu Ala Thr His Pro Glu Thr Val Gly Gln Val Thr Leu -40Arg Val Xaa Pro Val Ser Leu Glu Val Ser Ile Gln Met Cys Ala Ala - 30 -25 -20 Ala Ala Ala Phe Cys Leu Lys Xaa Xaa Gly Ala Asn Thr His Pro (2) INFORMATION FOR SEQ ID NO: 487: (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 86 amino acids (B) TYPE: AMINO ACID (D) TOPOLOGY: LINEAR (ii) MOLECULE TYPE: PROTEIN (vi) ORIGINAL SOURCE: (A) ORGANISM: Homo Sapiens (F) TISSUE TYPE: Brain (ix) FEATURE: (A) NAME/KEY: sig\_peptide (B) LOCATION: -64..-1 (C) IDENTIFICATION METHOD: Von Heijne matrix

Mst Ala Ala Ser Ser Ala Thr Pro Ala Pro Xaa Xaa Ser Gl<br/>n Arg Cys -60 -55 -50

seq GLGGAQLQGGAXG/RG

(D) OTHER INFORMATION: score 3.9

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 487:

- Gly Ala Asp Ala Gly Ser Ala Ala Arg Ile Val Phe Arg Trp Gly Arg
  -45 -40 -35
- Gly Arg Gly Ala Arg Ser Pro Glu Gly Ser Gly His His Gly Arg
  -30 -25 -20
- Ala Asn Ser Gly Leu Gly Gly Ala Gln Leu Gln Gly Gly Ala Xaa Gly
  -15 -10 -5
- Arg Gly Ser Met Ala Pro Leu Arg Ala Ser Ala Gly Gln Thr Arg Asp 1 5 10 15
- Gly Pro Thr Gln Pro Gly 20
- (2) INFORMATION FOR SEQ ID NO: 488:
  - (i) SEQUENCE CHARACTERISTICS:
    - (A) LENGTH: 50 amino acids
    - (B) TYPE: AMINO ACID
    - (D) TOPOLOGY: LINEAR
  - (ii) MOLECULE TYPE: PROTEIN
  - (vi) ORIGINAL SOURCE:
    - (A) ORGANISM: Homo Sapiens
    - (F) TISSUE TYPE: Brain
  - (ix) FEATURE:
    - (A) NAME/KEY: sig\_peptide
    - (B) LOCATION: -17..-1
    - (C) IDENTIFICATION METHOD: Von Heijne matrix
    - (D) OTHER INFORMATION: score 3.9

seq PLAGLAAAALGRA/PP

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 488:

Met Leu Arg Arg Pro Leu Ala Gly Leu Ala Ala Ala Leu Gly Arg

Ala Pro Pro Asp Gly Leu Leu Cys Ser Leu Pro Gly Val Ala Val Glu
1 5 10 15

Asp Pro Val Gln Asp Ser Ala Gly Phe Ser Phe Ser Leu Met Asp Arg

Pro Lys

- (2) INFORMATION FOR SEQ ID NO: 489:
  - (i) SEQUENCE CHARACTERISTICS:
    - (A) LENGTH: 53 amino acids
    - (B) TYPE: AMINO ACID
    - (D) TOPOLOGY: LINEAR
  - (ii) MOLECULE TYPE: PROTEIN

- (vi) ORIGINAL SOURCE:
  - (A) ORGANISM: Homo Sapiens
  - (F) TISSUE TYPE: Brain
- (ix) FEATURE:
  - (A) NAME/KEY: sig\_peptide
  - (B) LOCATION: -17..-1
  - (C) IDENTIFICATION METHOD: Von Heijne matrix
  - (D) OTHER INFORMATION: score 3.8

seq GFVAALVAGGVAG/VS

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 489:

Met Asp Arg Pro Gly Phe Val Ala Ala Leu Val Ala Gly Gly Val Ala
-15 -10 -5

Gly Val Ser Val Asp Leu Ile Leu Phe Pro Leu Asp Thr Ile Lys Thr
1 5 10 15

Arg Leu Gln Ser Pro Gln Gly Phe Ser Lys Ala Gly Gly Phe His Gly 20 25 30

Ile Tyr Ala Ser Trp

- (2) INFORMATION FOR SEQ ID NO: 490:
  - (i) SEQUENCE CHARACTERISTICS:
    - (A) LENGTH: 50 amino acids
    - (B) TYPE: AMINO ACID
    - (D) TOPOLOGY: LINEAR
  - (ii) MOLECULE TYPE: PROTEIN
  - (vi) ORIGINAL SOURCE:
    - (A) ORGANISM: Homo Sapiens
    - (F) TISSUE TYPE: Brain
  - (ix) FEATURE:
    - (A) NAME/KEY: sig\_peptide
    - (3) LOCATION: -21..-1
    - (C) IDENTIFICATION METHOD: Von Heijne matrix
    - (D) OTHER INFORMATION: score 3.8

seq SMDLLTLLFQRRS/HQ

- (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 490:
- Met Ile Val Trp Phe Glu Gly Ile Ser Met Asp Leu Leu Thr Leu Leu -20 -15 -10
- whe Gln Arg Arg Ser His Gln Val Thr Gln Leu Leu Val Ser Ser Thr  $\pm 5$  10
- Gly Asn Trp Leu Arg Gln Tyr Leu Cys Ala Ser Leu Thr Ile Ala Gly  $15\,$   $20\,$

Arg Arg

- (2) INFORMATION FOR SEQ ID NO: 491:
  - (i) SEQUENCE CHARACTERISTICS:
    - (A) LENGTH: 50 amino acids
    - (B) TYPE: AMINO ACID
    - (D) TOPOLOGY: LINEAR
  - (ii) MOLECULE TYPE: PROTEIN
  - (vi) ORIGINAL SOURCE:
    - (A) ORGANISM: Homo Sapiens
    - (F) TISSUE TYPE: Brain
  - (ix) FEATURE:
    - (A) NAME/KEY: sig\_peptide
    - (B) LOCATION: -20..-1
    - (C) IDENTIFICATION METHOD: Von Heijne matrix
    - (D) OTHER INFORMATION: score 3.8

seq ALDALMFPARRRA/AV

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 491:

Met Arg Thr Phe Val His Phe Ala Leu Asp Ala Leu Met Phe Pro Ala -20 -15 -10 -5

Arg Arg Ala Ala Val Thr Arg Leu Ser Glu Arg Leu Ser Leu Cys
1 5 10

Phe Cys Leu His Ser Arg Leu Gln Asp Pro Ala Ala Arg Pro Arg Pro
15 20 25

Ser Trp

- (2) INFORMATION FOR SEQ ID NO: 492:
  - (i) SEQUENCE CHARACTERISTICS:
    - (A) LENGTH: 99 amino acids
    - (B) TYPE: AMINO ACID
    - (D) TOPOLOGY: LINEAR
  - (ii) MOLECULE TYPE: PROTEIN
  - (vi) ORIGINAL SOURCE:
    - (A) ORGANISM: Homo Sapiens
    - (F) TISSUE TYPE: Brain
  - (ix) FEATURE:
    - (A) NAME/KEY: sig\_peptide
    - (B) LOCATION: -61..-1
    - (C) IDENTIFICATION METHOD: Von Heijne matrix
    - (D) OTHER INFORMATION: score 3.8 seq LVMTFLFRNGSLQ/EK

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(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 492:

Met Ala Ala Pro Pro Gln Leu Arg Ala Leu Leu Val Val Val Asn Ala
-60 -55 -50

Leu Leu Arg Lys Arg Arg Tyr His Ala Ala Leu Ala Val Leu Lys Gly
-45 -35 -30

Phe Arg Asn Gly Ala Val Tyr Gly Ala Lys Ile Arg Ala Pro His Ala
-25 -20 -15

Leu Val Met Thr Phe Leu Phe Arg Asn Gly Ser Leu Gln Glu Lys Leu -10 -5 1

Trp Ala Ile Leu Gln Ala Thr Tyr Ile His Ser Trp Asn Leu Ala Arg

Phe Val Phe Thr Tyr Lys Gly Leu Arg Ala Leu Gln Ser Tyr Ile Gln 20 25 30 36

Gly Pro Gly

# (2) INFORMATION FOR SEQ ID NO: 493:

- (i) SEQUENCE CHARACTERISTICS:
  - (A) LENGTH: 79 amino acids
  - (B) TYPE: AMINO ACID
  - (D) TOPOLOGY: LINEAR
- (ii) MOLECULE TYPE: PROTEIN
- (vi) ORIGINAL SOURCE:
  - (A) ORGANISM: Homo Sapiens
  - (F) TISSUE TYPE: Brain
- (ix) FEATURE:
  - (A) NAME/KEY: sig\_peptide
  - (B) LOCATION: -18..-1
  - (C) IDENTIFICATION METHOD: Von Heijne matrix
  - (D) OTHER INFORMATION: score 3.8

seq GXALGLLPSLAKA/ED

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 493:

Met Pro Val Asp Leu Gly Xaa Ala Leu Gly Leu Leu Pro Ser Leu Ala -15 -10 -5

Lys Ala Glu Asp Ser Gln Phe Ser Glu Ser Asp Ala Ala Leu Gln Glu  $\frac{1}{5}$  10

Glu Leu Ser Ser Pro Glu Thr Ala Arg Gln Leu Phe Arg Gln Phe Arg
15 20 25 30

Tyr Gln Val Met Ser Gly Pro His Glu Thr Leu Lys Xaa Leu Arg Lys 35 40 45

Leu Cys Phe Gin Trp Leu Gin Pro Glu Val His Thr Lys Glu Gly

50

55 60

(2) INFORMATION FOR	SEQ	Ţυ	NO:	494
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- (i) SEQUENCE CHARACTERISTICS:
  - (A) LENGTH: 139 amino acids
  - (B) TYPE: AMINO ACID
  - (D) TOPOLOGY: LINEAR
- (ii) MOLECULE TYPE: PROTEIN
- (vi) ORIGINAL SOURCE:
  - (A) ORGANISM: Homo Sapiens
  - (F) TISSUE TYPE: Brain
- (ix) FEATURE:

. 3

- (A) NAME/KEY: sig\_peptide
- (B) LOCATION: -72..-1
- (C) IDENTIFICATION METHOD: Von Heijne matrix
- (D) OTHER INFORMATION: score 3.8

seq LMGLALAVYKCQS/MG

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 494:

Met Asn Leu Phe Ile Met Tyr Met Ala Gly Asn Thr Ile Ser Ile Phe
-70 -65 -60

Pro Thr Met Met Val Cys Met Met Ala Trp Arg Pro Ile Gln Ala Leu
-55 -45

Met Ala Ile Ser Ala Thr Phe Lys Met Leu Glu Ser Ser Ser Gln Lys
-40 -35 -30 -25

Phe Leu Gln Gly Leu Val Tyr Leu Ile Gly Asn Leu Met Gly Leu Ala
-20 -15 -10

Leu Ala Val Tyr Lys Cys Gln Ser Met Gly Leu Leu Pro Thr His Ala
-5 1 5

Ser Asp Trp Leu Ala Phe Ile Glu Pro Pro Glu Arg Met Glu Ser Val 10 20

Val Glu Asp Cys Phe Cys Glu His Glu Lys Ala Ala Pro Gly Pro Tyr 25 30 35 40

Val Phe Gly Ser Tyr Leu His Pro Ser Leu Ser Pro Val Ala Pro Gln
45 50 55

His Thr Leu Lys Leu Ile Thr Tyr Val Lys Lys 60 65

## (2) INFORMATION FOR SEO ID NO: 495:

- (i) SEQUENCE CHARACTERISTICS:
  - (A) LENGTH: 102 amino acids
  - (B) TYPE: AMINO ACID

(D) TOPOLOGY: LINEAR

- (ii) MOLECULE TYPE: PROTEIN
- (vi) ORIGINAL SOURCE:
  - (A) ORGANISM: Homo Sapiens
  - (F) TISSUE TYPE: Brain
- (ix) FEATURE:
  - (A) NAME/KEY: sig\_peptide
  - (B) LOCATION: -51..-1
  - (C) IDENTIFICATION METHOD: Von Heijne matrix
  - (D) OTHER INFORMATION: score 3.8 seq NVLFVAGLAFVIG/LE
- (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 495:
- Met Ile Ser Leu Thr Asp Thr Gln Lys Ile Gly Met Gly Leu Thr Gly
  -50 -45 -40
- Phe Gly Val Phe Phe Leu Phe Phe Gly Met Ile Leu Phe Phe Asp Lys
  -35 -25 -20
- Ala Leu Leu Ala Ile Gly Asn Val Leu Phe Val Ala Gly Leu Ala Phe
  -15 -10 -5
- Val Ile Gly Leu Glu Arg Thr Phe Arg Phe Phe Phe Gln Lys His Lys  $1 \hspace{1cm} 5 \hspace{1cm} 10$
- Met Lys Ala Thr Gly Phe Phe Leu Gly Gly Val Phe Val Val Leu Ile 15 20 25
- Gly Trp Pro Leu Ile Gly Met Ile Phe Glu Ile Tyr Gly Phe Phe Leu 30 40 45

Leu Phe Arg Gly Leu Gly

- (2) INFORMATION FOR SEQ ID NO: 496:
  - (i) SEQUENCE CHARACTERISTICS:
    - (A) LENGTH: 53 amino acids
    - (B) TYPE: AMINO ACID
    - (D) TOPOLOGY: LINEAR
  - (ii) MOLECULE TYPE: PROTEIN
  - (vi) ORIGINAL SOURCE:
    - (A) ORGANISM: Homo Sapiens
    - (F) TISSUE TYPE: Brain
  - (ix) FEATURE:
    - (A) NAME/KEY: sig\_peptide
    - (B) LOCATION: -33..-1
    - (C) IDENTIFICATION METHOD: Von Heijne matrix
    - (D) OTHER INFORMATION: score 3.6 seq LAVFOMLKSMCAG/QR

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 496:

Met Ala Ala Ser Gly Ala Pro Arg Ile Leu Val Asp Leu Leu Lys Leu

Xaa Val Ala Pro Leu Ala Val Phe Gln Met Leu Lys Ser Met Cys Ala
-15 -10 -5

Gly Gln Arg Leu Ala Ser Glu Pro Gln Asp Pro Ala Ala Val Ser Leu 1 5 10

Pro Thr Ser Ser Gly 20

- (2) INFORMATION FOR SEQ ID NO: 497:
  - (i) SEQUENCE CHARACTERISTICS:
    - (A) LENGTH: 92 amino acids
    - (B) TYPE: AMINO ACID
    - (D) TOPOLOGY: LINEAR
  - (ii) MOLECULE TYPE: PROTEIN
  - (vi) ORIGINAL SOURCE:
    - (A) ORGANISM: Homo Sapiens
    - (F) TISSUE TYPE: Brain
  - (ix) FEATURE:
    - (A) NAME/KEY: sig\_peptide
    - (B) LOCATION: -26..-1
    - (C) IDENTIFICATION METHOD: Von Heijne matrix
    - (D) OTHER INFORMATION: score 3.6

seq ARSLLQFLRLVGQ/LK

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 497:

Met Ala Ser Val Ser Ser Ala Thr Phe Ser Gly His Gly Ala Arg Ser -25 -20 -15

Leu Leu Gln Phe Leu Arg Leu Val Gly Gln Leu Lys Arg Val Pro Arg -10 -5 5

Thr Gly Trp Val Tyr Arg Asn Val Gln Arg Pro Glu Ser Val Ser Asp

His Met Tyr Arg Met Ala Val Met Ala Met Val Ile Lys Asp Asp Arg 25 30 35

Leu Asn Lys Asp Arg Cys Val Arg Leu Ala Leu Val His Asp Met Ala 40 45 50

Glu Cys Ile Val Gly Asp Ile Ala Pro Ala Asp Gly
55 60 65

(2) INFORMATION FOR SEQ ID NO: 498:

(i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 24 amino acids (B) TYPE: AMINO ACID (D) TOPOLOGY: LINEAR (ii) MOLECULE TYPE: PROTEIN (vi) ORIGINAL SOURCE: (A) ORGANISM: Homo Sapiens (F) TISSUE TYPE: Brain (ix) FEATURE: (A) NAME/KEY: sig\_peptide (B) LOCATION: -16..-1(C) IDENTIFICATION METHOD: Von Heijne matrix (D) OTHER INFORMATION: score 3.6 seq LAVLLVLFTLNIL/KS (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 498: Met Trp Tyr Leu Ala Val Leu Leu Val Leu Phe Thr Leu Asn Ile Leu -15 Lys Ser Leu Tyr Trp Gln Pro Gly (2) INFORMATION FOR SEQ ID NO: 499: (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 58 amino acids (B) TYPE: AMINO ACID (D) TOPOLOGY: LINEAR (ii) MOLECULE TYPE: PROTEIN (vi) ORIGINAL SOURCE: (A) ORGANISM: Homo Sapiens (F) TISSUE TYPE: Brain (ix) FEATURE: (A) NAME/KEY: sig\_peptide (B) LOCATION: -42..-1 (C) IDENTIFICATION METHOD: Von Heijne matrix (D) OTHER INFORMATION: score 3.5 seq INSLLEXSSLSRC/LE (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 499: Met Phe Thr Phe Gly Arg Leu Phe Gln Ile Ile Thr Val Val Thr Cys -35

Leu Gln Phe Ile Gln Asp Cys Cys Ile His Ser Arg Gln Ile Asn Ser

Leu Leu Glu Xaa Ser Ser Leu Ser Arg Cys Leu Glu Val Pro Met Tyr

-10 -5 <sub>1</sub>

Val Lys Cys Ile Gly Ser Lys Ile Pro Leu 10 15

- (2) INFORMATION FOR SEQ ID NO: 500:
  - (i) SEQUENCE CHARACTERISTICS:
    - (A) LENGTH: 62 amino acids
    - (B) TYPE: AMINO ACID
    - (D) TOPOLOGY: LINEAR
  - (ii) MOLECULE TYPE: PROTEIN
  - (vi) ORIGINAL SOURCE:
    - (A) ORGANISM: Homo Sapiens
    - (F) TISSUE TYPE: Brain
  - (ix) FEATURE:
    - (A) NAME/KEY: sig\_peptide
    - (B) LOCATION: -51..-1
    - (C) IDENTIFICATION METHOD: Von Heijne matrix
    - (D) OTHER INFORMATION: score 3.5

seq VGTLCQLDWWIWG/GI

- (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 500:
- Met Ile Gln Asp Arg Asp Arg Cys Ala Gln Ala Ala Ala Val Ala Ala -50 -45 -40
- Val Gly Asn Leu Glu Pro Arg Gly Thr Pro Gly Pro Glu Asp Glu Ala
  -35 -25 -20
- Phe Cys Leu Pro Gly Cys Val Gly Thr Leu Cys Gln Leu Asp Trp Trp -15 -10 -5

Ile Trp Gly Gly Ile His Pro His Pro Thr Arg Lys Ala Trp

1 5 10

- (2) INFORMATION FOR SEQ ID NO: 501:
  - (i) SEQUENCE CHARACTERISTICS:
    - (A) LENGTH: 48 amino acids
    - (B) TYPE: AMINO ACID
    - (D) TOPOLOGY: LINEAR
  - (ii) MOLECULE TYPE: PROTEIN
  - (vi) ORIGINAL SOURCE:
    - (A) ORGANISM: Homo Sapiens
    - (F) TISSUE TYPE: Brain
  - (ix) FEATURE:
    - (A) NAME/KEY: sig\_peptide
    - (B) LOCATION: -31..-1
    - (C) IDENTIFICATION METHOD: Von Heijne matrix
    - (D) OTHER INFORMATION: score 11.3

seq LLLCLLWIGYSQG/TT

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 501:

Met Lys Ile Ile Phe Pro Ile Leu Ser Asn Pro Val Phe Arg Arg Thr -30 -25 -20

Val Lys Leu Leu Cys Leu Leu Trp Ile Gly Tyr Ser Gln Gly Thr
-15 -5

Thr His Val Leu Arg Phe Gly Gly Ile Phe Glu Tyr Val Glu Ser Gly
5 10

- (2) INFORMATION FOR SEQ ID NO: 502:
  - (i) SEQUENCE CHARACTERISTICS:
    - (A) LENGTH: 57 amino acids
    - (B) TYPE: AMINO ACID
    - (D) TOPOLOGY: LINEAR
  - (ii) MOLECULE TYPE: PROTEIN
  - (vi) ORIGINAL SOURCE:
    - (A) ORGANISM: Homo Sapiens
    - (F) TISSUE TYPE: Brain
  - (ix) FEATURE:
    - (A) NAME/KEY: sig\_peptide
    - (B) LOCATION: -26..-1
    - (C) IDENTIFICATION METHOD: Von Heijne matrix
    - (D) OTHER INFORMATION: score 6.6 seq LFWLASGWTPAFA/YS
  - (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 502:

Met Val Ser Arg Met Val Ser Thr Met Leu Ser Gly Leu Leu Phe Trp -25 -20 -15

Leu Ala Ser Gly Trp Thr Pro Ala Phe Ala Tyr Ser Pro Arg Thr Pro -10 -5 1 5

Asp Arg Val Ser Glu Ala Asp Ile Gln Arg Leu Leu His Gly Val Met 10 15 20

Glu Gln Leu Gly Ile Ala Arg Pro Arg 25 30

- (2) INFORMATION FOR SEQ ID NO: 503:
  - (i) SEQUENCE CHARACTERISTICS:
    - (A) LENGTH: 46 amino acids
    - (B) TYPE: AMINO ACID
    - (D) TOPOLOGY: LINEAR
  - (ii) MOLECULE TYPE: PROTEIN

- (vi) ORIGINAL SOURCE:
  - (A) ORGANISM: Homo Sapiens
  - (F) TISSUE TYPE: Brain
- (ix) FEATURE:
  - (A) NAME/KEY: sig\_peptide
  - (B) LOCATION: -24..-1
  - (C) IDENTIFICATION METHOD: Von Heijne matrix
  - (D) OTHER INFORMATION: score 4.8 seq ATMVSGSSGLAXA/RL

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 503:

Met Thr Ala Thr Leu Ala Ala Ala Ala Asp Ile Ala Thr Met Val Ser

Gly Ser Ser Gly Leu Ala Xaa Ala Arg Leu Leu Ser Arg Xaa Ser Ser

Cys Arg Arg Met Glu Phe Gly Ile Val Pro Thr Gln Pro Arg 10 15 20

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(51) International Patent Classification <sup>6</sup> : C12N 15/12, C07K 14/47, C12N 15/10, 15/11	A3	<ul> <li>(11) International Publication Number: WO 99/06552</li> <li>(43) International Publication Date: 11 February 1999 (11.02.99)</li> </ul>
(21) International Application Number: PCT/I  (22) International Filing Date: 31 July 1998  (30) Priority Data: 08/905,223 1 August 1997 (01.08.97)  (71) Applicant (for all designated States except US): [FR/FR]; 24, rue Royale, F-75008 Paris (FR).  (72) Inventors; and WARDS, Jean-Baptiste [FR/FR]; 8, rue Grégoin F-75006 Paris (FR). DUCLERT, Aymeric [FR/rue Victorine, F-94100 Saint-Maur (FR). LACRE [FR/FR]; 93, route de Vourles, F-69230 Saint-C (FR).  (74) Agent: MARTIN, Jean-Jacques; Cabinet Regin avenue Kléber, F-75116 Paris (FR).	GENSE GENSE	BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GF, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SI TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, ARIPP patent (GH, GM, KE, LS, MW, SD, SZ, UG, ZW), Eurasia patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), Europea patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GF, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CI CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG).  Published  With international search report.  (88) Date of publication of the international search report: 22 April 1999 (22.04.9)
and genomic DNAs corresponding to the 5' ESTs. The	encoding 5' ESTs	secreted proteins are disclosed. The 5' ESTs may be to obtain cDNA may also be used in diagnostic, forensic, gene therapy, and chromoson e obtained using the 5' ESTs. The 5' ESTs may also be used to design

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Internal Application No. PCT/18 98/01236

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According to	o International Patent Classification (IPC) or to both national cla	assification and IPC	
	SEARCHED		
IPC 6	ocumentation searched (classification system followed by class C12N C07K	ification symbols)	
Documentat	tion searched other than minimum documentation to the extent	that such documents are included in the field	
Electronic da	ata base consulted during the international search (name of da	ita base and, where practical, search terms us	sed)
C. DOCUME	NTS CONSIDERED TO BE RELEVANT		
Category *	Citation of document, with indication, where appropriate, of the	ne relevant passages	Relevant to claim No.
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	vol. 4, no. 3, July 1993, page XP000645060 see the whole document	es 256-267,	
A	ADAMS M D ET AL: "RAPID CDNA (EXPRESSED SEQUENCE TAGS) FROM DIRECTIONALLY CLONED HUMAN INF CDNA LIBRARY" NATURE GENETICS, vol. 4, no. 4, August 1993, pa STANDARD, XP002064427 see the whole document	1 A FANT BRAIN	
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X Furthe	er documents are listed in the continuation of box C.	X Patent family members are liste	id in annex.
A* document consider E* earlier do filing dail L* document which is citation of document other me	it which may throw doubts on priority claim(s) or cided to establish the publication date of another or other special reason (as specified) it referring to an oral disclosure, use, exhibition or ears.	"T" later document published after the in or pnorty date and not in conflict will cited to understand the principle or invention."  X' document of particular relevance; the cannot be considered novel or can involve an inventive step when the involve an inventive step when the cannot be considered to involve an document of particular relevance; the cannot be considered to involve an document is combined with one or ments.	th the application but theory underlying the sclaimed invention to be considered to document is taken alone e claimed invention inventive step when the
later tha	it published pnor to the international filling date but in the priority date claimed	ments, such combination being obv in the art.  *&* document member of the same pater	
	November 1998	Date of mailing of the international at 1 7, 02, 99	
lame and ma	siling address of the ISA  European Patent Office, P.B. 5818 Patentiaan 2  NL - 2280 HV Rijswijk	Authorized officer	
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International Application No PC | / IB 98/01236

	·	PC1/1B 98/01236
C.(Continu	ation) DOCUMENTS CONSIDERED TO BE RELEVANT	
Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	EP 0 279 582 A (BAYLOR COLLEGE MEDICINE) 24 August 1988 see the whole document	12,13
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A	LOCKHART D J ET AL: "EXPRESSION MONITORING BY HYBRIDIZATION TO HIGH-DENSITY OLIGONUCLEOTIDE ARRAYS" BIO/TECHNOLOGY, vol. 14, no. 13, December 1996, pages 1675-1680, XP002022521 see the whole document	35-37
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Α .	KATO S. ET AL.: "Construction of a human full-length cDNA bank" GENE, vol. 150, 1994, pages 243-250, XP002081364 cited in the application	
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A	CARNINCI P. ET AL.: "High-efficiency full-length cDNA cloning by biotinylated CAP trapper" GENOMICS, vol. 37, no. 3, 1 November 1996, pages 327-336, XP002081729 cited in the application	
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Internacional application No

PCT/IB 98/01236

Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)
This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:
Claims Nos.: because they relate to subject matter not required to be searched by this Authority, namely:
Claims Nos.: because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:
3. Claims Nos.: because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).
Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)
This International Searching Authority found multiple inventions in this international application, as follows:
Please see additional sheet.
As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
2. As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:
4. X No required additional search fees were timely paid by the applicant. Consequently, this international Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:  1-37 all partially
Remark on Protest  The additional search fees were accompanied by the applicant's protest.  No protest accompanied the payment of additional search fees.

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PCT/18 98/01236

CICoptie	Alian Danimenta and September 19 pr	PC1,1B 98/01236
Category *	ation) DOCUMENTS CONSIDERED TO BE RELEVANT	
Jakeyory	Chation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No
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А	TASHIRO K. ET AL.: "Signal sequence trap: a cloning strategy for secreted proteins and type I membrane proteins" SCIENCE, vol. 261, 30 July 1993, pages 600-603, XP000673204	
A	YOKOYAMA-KOBAYASHI M. ET AL.: "A signal sequence detection system using secreted protease activity as an indicator" GENE, vol. 163, 1995, pages 193-196, XP002053953	
A	HEIJNE VON G.: "A new method for predicting signal sequence cleavage sites" NUCLEIC ACIDS RESEARCH, vol. 14, no. 11, 1986, pages 4683-4690, XP002053954 cited in the application	
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#### FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

1. Claims: Invention 1: claims 1-37 all partially

Nucleic acid comprising the sequence as in Seq.ID:38, complementary sequence, fragments, hybridizing sequences. Polypeptide comprising a signal peptide encoded by said nucleotide sequence. Vector encoding a fusion protein comprising said signal peptide. A method of directing the extracellular secretion of a polypeptide by means of said vector. Method of importing a polypeptide into a cell by means of said signal peptide. A method for making a cDNA encoding a secretory protein, partially encoded by said nucleotide sequence, corresponding cDNA. Polypeptide encoded by said nucleotide sequence, comprising a sequence as in Seq.ID:271, method of making said polypeptide. Method of obtaining a promoter located upstream of said nucleotide sequence, promoter thereof.

2. Claims: Invention 2-233: claims 1-37 all partially

Inventions 2-233: Idem as subject 1 but limited to each of the DNA sequences as in Seq.ID:39-271, and corresponding polypeptides, where invention 2 is limited to Seq.ID:39 and 272, invention 3 is limited to Seq.ID:40 and 273,....., invention 233 is limited to Seq.ID:270 and 503).

For the sake of conciseness, the first subject matter is explicitly defined, the other subject matters are defined by analogy thereto.

II. nation on patent family members

Internarianal Application No
PCT/1B 98/01236

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